MENTAL, COGNITIVE, PHYSICAL, AND NEUROBIOLOGICAL HEALTH IN AGED INDIVIDUALS FOLLOWING THE EXPOSURE TO POTENTIALLY TRAUMATIC EVENTS

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Prof. Dr. Dr. Andreas Maercker (main supervisor)

Prof. Dr. Markus Landolt

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ABSTRACT

The exposure to potentially traumatic events can serve as an antecedent of health alterations in both short- and long-term. More precisely, a range of health alterations have previously been observed in the domains of mental and physical health as well as in neurodegenerative cognitive conditions. Nevertheless, from pertinent studies it is evident that not all individuals go on to develop health alterations following the exposure to potentially traumatic events. This heterogeneity may be due to the impact of factors during and after the exposure to potentially traumatic events. Mediating factors following the exposure to potentially traumatic events such as the exposure to subsequent life stressors and the perceived social acknowledgement are further assumed to profoundly influence health over the life course. An emerging study group of interest in this context are individuals with a history of child welfare care as these individuals were at increased risk to experience severe forms of child maltreatment. Nevertheless, most studies that investigate the long-term potential health alterations and mitigating factors associated with potentially traumatic events and child maltreatment within welfare care settings have focused on young to middle-aged adults, whereas findings in aged individuals are sparse. This is also true for the investigation of neurobiological health associates following the exposure to potentially traumatic events and in association with probable post-traumatic stress disorder (PTSD) symptoms in aged individuals.

This cumulative thesis contributes to the body of knowledge by examining health associates in two samples of aged individuals following the exposure to potentially traumatic childhood events with a particular focus on maltreatment in the context of child welfare care. More precisely, Manuscript 1 ($N = 238$) and Manuscript 2 ($N = 253$) examined health associates in the domains of mental, cognitive, and physical functioning following the exposure to child maltreatment and within the context of child welfare care. Results revealed that individuals with higher levels of exposure to child maltreatment reported higher levels of lifetime PTSD

symptomatology and more stressful life events independent of a history of child welfare care (Manuscript 1). Results of Manuscript 2 revealed that lower levels of physical and cognitive functioning in older age were particularly pronounced in individuals with a history of child welfare care. Additionally, within the two manuscripts factors influencing these health associates were examined. Social acknowledgement following the exposure to potentially traumatic events mediated the relationship between child maltreatment and lifetime PTSD, but only in individuals without history of child welfare care (Manuscript 1). Manuscript 2 reveals that life stressors mediated the relationship between exposure to child maltreatment and subjective physical health in the group of individuals with a history of child welfare care.

Within Manuscript 3 the neural underpinnings following the exposure to a potentially traumatic event and in association with probable PTSD symptoms were investigated using resting-state functional magnetic resonance imaging (rs-fMRI) connectivity ($N = 110$). Results revealed lower functional connectivity within the Default Mode Network in individuals reporting probable PTSD symptoms and higher functional connectivity within the Salience Network in individuals following the exposure to potentially traumatic events.

The discussion of this cumulative thesis provides avenues for future research to probe neurobiological signatures following the exposure to potentially traumatic events and in association with probable PTSD symptoms. Furthermore, thoughts on how to study amendments in perceived levels of social acknowledgement are provided. Clinical implications for this research include the treatment of individuals following the exposure to child maltreatment, the assessment of lifetime trauma history and recommendations for the amelioration of child protective policies and the enhancement of insurance policies.

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LIST OF ABBREVIATIONS

CG	Control Group
CM	Child Maltreatment
CSMP	Compulsory Social Measure and Placements
DMN	Default Mode Network
DSM	Diagnostic and Statistical Manual of Mental Disorders
ELA	Early Life Adversity
FC	Functional Connectivity
fMRI	Functional Magnetic Resonance Imaging
ICD	International Classification of Diseases
ICN	Intrinsic Connectivity Networks
LHAB	Longitudinal Healthy Aging Brain Database Project
LME	Linear Mixed Effects
MANOVA	Multivariate Analysis of Variance
MRI	Magnetic Resonance Imaging
NRP76	National Research Program 76
PTSD	Post-Traumatic Stress Disorder
RG	Risk Group
rs-FC	Resting-state functional connectivity
rs-fMRI	Resting-state Functional Magnetic Resonance Imaging
SN	Salience Network
SPSS	Statistical Package of Social Sciences
WHO	World Health Organization

1 INTRODUCTION

A factor that has repeatedly been linked to negative health implications is the exposure to potentially traumatic events over the life span. Particularly, exposure to early-life adversity, such as child maltreatment, is associated with a decline in mental, cognitive, and physical health (Archer et al., 2017; Steine et al., 2017; Wang et al., 2019). Within the last decade an increasing number of studies have started to examine health associates following exposure to child maltreatment in individuals who have been exposed to severe forms of maltreatment during their time in child welfare care (Carr et al., 2020b). However, so far, most research studies were conducted with young to middle-aged adults and findings regarding long-term health associates of child maltreatment in individuals of older age, are sparse (Carr et al., 2019; Jackson et al., 2011; Lueger-Schuster et al., 2018; Salazar et al., 2011; Sigal et al., 2003). At present, many individuals with a childhood history in the Swiss welfare care system have reached older age, presenting a unique window of time to examine long-term health associates following the exposure to child maltreatment in this Swiss older adult population. Further, more basic research on neurobiological signatures following the exposure to potentially traumatic events and in association with probable post-traumatic stress disorder (PTSD) symptoms over the life course is needed to understand the pathogenesis associated with post-traumatic stress responses that persist into older age.

More precisely, the aim of this cumulative thesis is to examine mental, cognitive, physical, and neurobiological health associates following the exposure to potentially traumatic events, with a focus on child maltreatment, until older age. Manuscript 1 examined the manifestation of lifetime PTSD symptomatology following the exposure to child maltreatment, particularly within the context of child welfare care, while accounting for perceived social acknowledgement following this exposure and presence of subsequent life stressors.

Manuscript 2 concentrated on cognitive and physical functioning in older individuals with a history of child welfare care in comparison to individuals without such history and further investigates the mediating role of life stressors on the relationship. Manuscript 3 reveals neurobiological underpinnings in the form of altered functional connectivity (FC) between regions commonly implicated in PTSD in the context of aging while addressing the exposure to potentially traumatic events and probable PTSD symptoms as influencing factors.

The synopsis starts by introducing the background of the present thesis. Chapter 1 provides a detailed overview of the current state of research and theoretical considerations regarding the exposure to potentially traumatic events and child maltreatment on mental, cognitive, and physical functioning as well as on neurobiological underpinnings over the life course and until older age. Following this presentation of the empirical and theoretical background, Chapter 2, the present thesis, addresses the main research questions and outlines the research projects. Further, the three manuscripts underlying the present thesis are briefly summarized regarding their objectives, main findings, and conclusions. Chapter 3 is dedicated to thoroughly discuss present findings by also providing recommendations for future research as well as potential clinical implications and recommendation for policy and practice. The last chapter (Chapter 4) provides the three full-length manuscripts subject to this cumulative dissertation.

2 THEORETICAL BACKGROUND

The following chapter will present theoretical and empirical research considerations central to this cumulative thesis. More precisely, this chapter will start off by defining exposure to potentially traumatic events and exposure to child maltreatment within the context of child welfare care, the latter of which is central to Manuscript 1 and 2. Furthermore, health associates following the exposure to child maltreatment, relevant to Manuscript 1 and 2, will be outlined in the following order: mental health including lifetime PTSD, and cognitive and physical functioning in older age. This is followed by a description of explanatory theoretical models of factors that influence the longer-term outcomes following exposure to child maltreatment including the theories of cumulative disadvantage and stress-sensitivity. Furthermore, given the nature of the specific sample underlying Manuscript 1 and 2 - individuals affected by Swiss child welfare care practices - and its recent societal reappraisal, theoretical consideration stemming from the socio-interpersonal model following the exposure to potentially traumatic events will be provided. Finally, central to Manuscript 3, previous research findings and theoretical considerations of the neurobiological underpinnings of aging and exposure to potentially traumatic events in association with probable PTSD symptoms are outlined.

2.1 Exposure to Potentially Traumatic Events

According to the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) the exposure to potentially traumatic events is defined as the "exposure to threatened death, serious injury or sexual violence" (DSM-5: American Psychiatric Association [APA], 2013). The *International Classification of Diseases* (ICD)-10 provides more global guidelines regarding what constitutes an event to be traumatic: "Exposure to a stressful event or situation (either short or long lasting) of exceptionally threatening or catastrophic nature, which is likely to cause pervasive distress in almost anyone" (ICD-10: World Health Organization [WHO], 2014). The definition or guideline for the exposure to potentially traumatic events (termed

'Criterion A' in the above-mentioned diagnostic manuals) has undergone numerous alterations since its initial conceptualization in the third edition of the *Diagnostic and Statistical Manual of Mental Disorders* as an event that is outside "the range of usual human experience" (DSM-III; APA, 1980; Hyland et al., 2020). Following the current state of the field, a potentially traumatic event can be experienced or witnessed first-hand, and can also affect individuals who were indirectly confronted with the nature of the event (APA, 2013) and is typically conceptualized as belonging to one of the following categories: disasters (e.g., natural disasters, armed conflicts), interpersonal violence (e.g., sexual abuse, physical abuse), serious accidents (e.g., automobile accident), and sudden death (e.g., severe illness) (Ouagazzal & Boudoukha, 2019).

Exposure to potentially traumatic events is likely to occur in most individuals at some point in their lives. For instance, a mental health survey by the World Health Organization found exposure rate to at least one traumatic event of 70%, with an average exposure rate to potentially traumatic events of 3.2 per person (Kessler et al., 2017), while in another epidemiological study reported that two out of three people will be exposed to at least one traumatic event during their life course (Norris, 1992; Resnick et al., 1993). A major concern in the field of research following the exposure to potentially traumatic events has been to understand why some individuals develop health consequences following exposure (Bellis et al., 2019), while other individuals seem to be largely unaffected (Bonanno, 2004). Several phenotypic factors have been studied aiming to explain the observed heterogeneity in consequences following the exposure to a potentially traumatic event (Kaysen et al., 2010; Lima et al., 2014; Perrin et al., 2014).

One factor that has been repeatedly linked to adverse health consequences following the exposure to potentially traumatic events is the effect of timing, or age at which the trauma occurs (Dunn et al., 2017; Ogle et al., 2013; McEwen, 2004). For instance, a study investigating

the developmental impact of timing of potentially traumatic events revealed that in later life (mean age 60.83 years), individuals with a history of early trauma exposure reported more symptom distress compared to individuals who were exposed to potentially traumatic events during adulthood (Ogle et al., 2013). Accordingly, it has been suggested that exposure to potentially traumatic events during important developmental periods may increase susceptibility to post-traumatic stress sequelae (Springer et al., 2003). As such previous research studies have shown that particularly early exposure to potentially traumatic events such as child maltreatment are related to adverse health outcomes in later life (Kaplow & Widom, 2007; Kisely et al., 2018). Hence, during investigations of health associates following potentially traumatic events, attention should be drawn to child maltreatment, which might leave behind particularly profound "blueprints" (Dunn, et al., 2017; Dunn et al., 2018).

2.1.1 Exposure to Child Maltreatment

The terminology *child maltreatment* refers to the World Health Organization description for abuse and neglect that is experienced before the age of 18 years (WHO, 2020). More precisely, child maltreatment is an umbrella term including various types of abuse, exploitation, negligence, and neglect that are associated with detrimental effects on the development, survival, and health of the child (WHO, 2020). According to Barnett et al. (1993) and in agreement with current conceptualizations, child maltreatment is oftentimes distinguished according to the following four categories: a) physical abuse (i.e., physical harm in form of beating, kicking, punching), b) sexual abuse (i.e., sexual harassment, indecent exposure, sexual exploitation), c) emotional neglect (i.e., invalidating and ignoring of the child's needs), and d) emotional abuse (i.e., verbal aggression, insulting, yelling and rejection of the child). Child maltreatment is not only assessed by researchers but is also of great relevance for social systems due to legal matters and for the treatment of affected individuals by mental health professionals.

Global investigations revealed that child maltreatment is highly prevalent. A recent Swiss epidemiological study observed that in a three-month period 10,335 cases were reported to child protective services with the dark figure being potentially even higher (Jud et al., 2021). In a German population study, the exposure to severe emotional abuse was 2.6%, for severe physical abuse 3.3%, for severe sexual abuse 2.3%, for severe emotional neglect 7.1%, and severe physical neglect 9% (Witt et al., 2017). These higher rates of exposure to neglect have further been confirmed in a nationwide prevalence study conducted in the Netherlands (56% exposure to neglect and 4% exposure to sexual abuse) (Euser et al., 2010). Furthermore, different cohorts may have been affected by different types and dimensions of exposure to child maltreatment, partly tracing back to environmental circumstances (e.g., World War II, Dutch famine) (Glaesmer et al., 2010; Roseboom et al., 2006).

One cohort of individuals emphasized in this thesis are individuals affected by welfare care in their childhood and/or adolescence. More precisely, within the last decade, an increasing number of individuals with a history of institutional upbringing have come forward with their experiences of child maltreatment across various international child welfare care settings (Carr et al., 2020b). As such, a more concrete picture has emerged on the extent and nature of child maltreatment that individuals have endured. The following section outlines empirical findings on the exposure to child maltreatment in the context of child welfare care.

2.1.2 Exposure to Child Maltreatment in the Context of Child Welfare Care

Within the last century, many children were placed by central governments, local authorities, and religious affiliations into various child welfare care settings (Gallagher, 1999). These settings included childcare centers, orphanages, boarding schools, residential care centers, reformatories, young offender institutions, farming facilities, health-care facilities, and churches. Over time, several reports of child maltreatment in these settings have become

publicized, but the investigation of child maltreatment within these institutions has been largely denied and/or underreported (Biehal, 2014; Gallagher, 1999). However, from pertinent reports within the last decade, it has become evident that within these settings, affected individuals were prone to experience severe forms of child maltreatment (the Vienna Institutional Abuse-Study, Lueger-Schuster et al., 2018; the Commission to Inquire into Child Abuse, Ryan, 2009; National Research Program 76, Thoma et al., 2021a). Results of a systematic review of child abuse in long-term care indicated that children were exposed to rates as high as 67% for sexual abuse, 63% for physical abuse, and 71% for emotional abuse (Carr et al., 2020b). Given the nature and extent of child maltreatment across institutional settings, child maltreatment executed by individuals working with children in institutional settings has been termed institutional abuse (Gallagher, 2000; Lueger-Schuster et al., 2018).

Institutional abuse is thought to differ from intrafamilial abuse (i.e., perpetrators stemming from the family of origin) regarding several factors. First, the relationship with the perpetrator is by nature fundamentally different, as within the context of welfare care perpetrators are not family members, but adults who were ordered to be responsible for the child's welfare with seemingly unbreakable level of power over their child in custody – being their legal guardian, teacher, and determinant for their future career (Stein, 2006; Wolfe et al., 2003). Furthermore, from pertinent reports it appears that severe forms of child maltreatment have also been executed by peers placed within the very same institution (Stein, 2006). Additionally, minors placed within institutional settings oftentimes already came with a history of child maltreatment from their family of origin (Greeson et al., 2011). Other factors include the often-encountered frequent change of caregivers within the institutional setting (i.e., child's dependency on good will, deferral of responsibility and trust) (Carr et al., 2020b), the young age of the person in care (i.e., need for developmental scaffolding) (Gallagher, 2000) and the

economic context of the time (i.e., weak yields, economic instability due to war and poverty) (Leuenberger & Seglias, 2008).

Apart from this, the nature of exposure to child maltreatment in child welfare care settings was often very severe, frequent, and protracted (Carr et al., 2020b). For instance, Lueger-Schuester and colleagues (2018) observed that survivors of institutional abuse reported higher exposure to child maltreatment and more severe forms of exposure to all types of child maltreatment in comparison to their control group with no history of institutional upbringing. Importantly these differences remained considerable even when comparing only severely exposed individuals of the control group with the survivors of institutional abuse. Although the system was originally created to improve the protection of the child, individuals who have attempted to disclose the severe forms of institutional abuse and neglect were dismissed as 'children', punished, and disbelieved, leaving them with no prospect of help (Hill, 2004). This might have been further exacerbated by the societal context of the time - stigmatization of children placed within welfare care systems in contrast to the value of institution within the society (Wolfe et al., 2006).

In addition to the above outlined factors, research findings with survivors of child welfare care practices have revealed various significant associations between exposure to child maltreatment and health outcomes (i.e., mental, cognitive, and physical health) as well as problems with psychosocial adjustment later in life (Carr et al., 2020b; Lueger-Schuster et al., 2018; Thoma et al., 2021a). However, these associations have predominantly been investigated in young to middle-aged adults, with a poor understanding of longer-term associations of child maltreatment in individuals of older age. As Manuscripts 1 and 2 examine health associates following the exposure to child maltreatment within Swiss child welfare care setting, the next section describes an outlook on the historical background, forms of Swiss child welfare care practices and the recent reappraisal movement.

2.1.2.1 Child Welfare Care Practices in Switzerland

In Switzerland child welfare care practices, also termed compulsory social measure and placements (CSMP), were ordered from the administrative authorities to counteract the growing threat faced due to weak economic yields, lengthy famines and increasing impoverishment (Federal Office of Justice, 2020). Grounds for CSMP were parents who did not meet societal standards of the time (i.e., single motherhood, poverty, mental health issues of the parents) or moral reservations about the behavior of the minors themselves (i.e., individuals were seen as "work-shy" or "dissolute"). In Switzerland, various form of CSMP were implemented. For instance, forced placements into closed penal facilities, detention centers, and psychiatric institutions, where forced measures such as enforced adoptions and compulsory medical procedures (e.g., mandatory sterilization, forced abortion or compulsory drugging) were executed (Federal Office of Justice, 2020). Another form of CSMP was to command the placement of minors into designated foster care settings. Typical foster care settings were local farms, children's homes, baby nurseries or approved schools. In these institutions the children were forced to make a living by means of heavy physical work, mostly compromised of farming and animal husbandry, which were given the German term *Verdingkinder* [former indentured child laborers] (Leuenberger & Seglias, 2013).

In 2010, the federal councilor Eveline Widmer-Schlumpf was the first to apologize to Swiss individuals affected by CSMP (White, 2010). This has largely been seen as the starting point of reappraisal of the Swiss history of CSMP and the association of severe forms of child maltreatment within these settings. Thereupon, in 2015 an independent expert commission was formed with the task to conduct scientific reviews on the CSMP measures and by 2006 it was agreed upon by the Swiss government to provide affected individuals with a solidarity payment contribution of 25 000 Franken (Federal Office of Justice, 2020). Individuals affected by

CSMP applied for this solidary payment between January 2017 and March 2018 at the Federal Ministry of Justice.

Following the reports stemming from the independent expert commission the Federal Council further initiated the National Research Program (NRP) 76 by the Swiss National Science Foundation. The NRP76 “Welfare and Coercion- Past Present Future” comprises a total 27 research projects conducted between 2018 and 2023 with the aim to further knowledge on mechanisms, characteristics, and consequences of practices exhibited in CSMP (NRP76 "Welfare and Coercion – Past, Present and Future", 2021).

So far, most research has been conducted with former indentured child laborers (Burri et al., 2013; Höltge et al., 2018; Maercker et al., 2016), which is just one subgroup of individuals affected by the more global CSMP measures, which took place in Switzerland within the last century. Furthermore, studies conducted with indentured child laborers have largely been missing a control group which hinders more general conclusions on provided findings (Burri et al., 2013; Höltge et al., 2018). As a substantial part of individuals affected by Swiss welfare care practices are now 50 years or older, the NRP76 project provides researchers with an unmatched opportunity to examine longer-term health associations of institutional upbringing and exposure to child maltreatment in older age adults.

2.2 Health Associates Following the Exposure to Child Maltreatment

The exposure to child maltreatment is seen as a major public health issue (Arnow, 2004; Springer, et al., 2003). Previous research studies have reported a strong association between the exposure to child maltreatment and various health problems in later life. In fact, observed consequences are diverse and vary from mental health problems such as depression (Weich et al.,2018), PTSD (Kessler et al., 2010) and substance use disorders (MacMillan et al., 2001) to physical health problems (e.g., more frequent illness and increased risk of injury due to

engagement in risky behaviour) (Kendall-Tackett, 2002), and increased rates of age-related decline (e.g., lower cognitive performances in older age) (Short & Baram, 2019). When examining the relationship between exposure to child maltreatment and health several researchers argue for the existence of a dose-response relationship, with more severe child maltreatment exposure leading to more adverse outcomes in adulthood (Steine et al., 2017). The following section will first outline studies investigating the association between exposure to child maltreatment and probable PTSD and then will describe observations on cognitive and physical functioning following exposure to child maltreatment.

2.2.1 Post-traumatic Stress Disorder Following the Exposure to Child Maltreatment

A strong body of evidence demonstrates that following the exposure to child maltreatment individuals may be more inclined to develop PTSD (Kessler et al., 2010; Messman-Moore & Bhuptani, 2017; Yehuda et al., 2001) – a trauma-specific disorder with debilitating symptoms (American Psychological Association, 2013). The diagnosis of PTSD was first introduced in 1980, given the observation of a debilitating symptom sequalae in veterans returning from the Vietnam and Gulf war (Diagnostic and Statistical Manual of Mental Disorders: DSM-III, APA, 1980; Hendin & Haas, 1985) and years later was recognized in the ICD (WHO, 1992). In order to meet a PTSD diagnosis following the exposure to potentially traumatic events, PTSD symptoms of four symptom categories must be experienced for a minimum of four weeks: 1) re-experiencing of the traumatic events (e.g., intrusions, flashbacks, recurring dreams), 2) avoidance of traumatic reminders and numbing of emotions, 3) increased arousal or heightened sense of threat, and 4) negative thoughts and mood as well as functional impairment cause by the above introduced symptoms (APA, 2013; WHO, 2014). Prevalence rates of PTSD in the general population are estimated between 1.1% to 2.9% (Trautmann & Wittchen, 2018). However, even higher prevalence rates (30% to 38%) (Widom, 1999) and more severe PTSD

symptoms have been observed (Briere & Spinazzola, 2005; Cloitre et al., 2009) following interpersonal traumatic events and particularly when experienced during childhood.

Most research on exposure to potentially traumatic events during childhood and/or adolescence has focused on health associates following the exposure to child sexual and physical abuse (Yehuda et al., 2001), with exposure to child emotional abuse and neglect being a more recent topic of interest (Fung et al., 2020). This may be due to the fact that the DSM-5 does not include the exposure to emotional abuse and neglect within their criterium A- "Exposure to actual or threatened death, serious injury, or sexual violence" (APA, 2013). Nevertheless, there is a substantial body of research demonstrating the development PTSD symptoms following the exposure to emotional abuse and neglect in childhood and/or adolescence (Schneider et al., 2007; Spertus et al., 2003).

Furthermore, several researchers have pointed out that the combination of multiple types of abuse and neglect might even lead to more devastating long-term health associates in later life, in a dose-dependent manner (Norman et al., 2012; Steine et al., 2017). More precisely, the experience of more child maltreatment is associated with a higher risk to develop PTSD symptoms. Moreover, cumulative exposure to child maltreatment might increase the risk for subsequent maladaptive behavioral patterns (e.g., alcohol misuse) and high levels of distress (Conroy et al., 2009; Shin et al., 2015) influencing the manifestation of probable PTSD (Steine et al., 2017).

A group of individuals who were at a heightened risk of cumulative and diverse exposure to child maltreatment are those with a history of child welfare care and might therefore have increased susceptibility for the development of PTSD (Lueger-Schuster et al., 2018; Car et al. 2020b). According to a systematic review on the health associates of child abuse in long-term care, prevalence rates of PTSD ranged from 7% to 74%, for current and lifetime PTSD (Carr et al., 2020b). With a mean prevalence of 51% it was concluded that

lifetime and current PTSD were above average in individuals affected by institutional abuse compared to the general population. This is particularly evident in a study by Lueger-Schuster and colleagues (2018) who reported prevalence of 56.4% for lifetime and 35.6% for current PTSD compared to rates of < 1% in their non-institutionalized comparison group. A key finding revealed that the manifestation of PTSD symptoms was directly associated with rates of exposure to emotional and sexual abuse, consistent with the argument that particularly high levels of exposure to various types of child maltreatment are thought to be detrimental to the health of survivors of institutional abuse (Lueger-Schuster et al., 2018). However, most research regarding the effects of institutional abuse on probable PTSD symptoms has focused on young to middle-aged adults (Carr et al., 2020b, Jackson et al., 2011, Salazar et al., 2011) and longer-term association studies are sparse.

Furthermore, it has been reported that PTSD symptom expression is thought to change throughout the life course (Averill & Beck, 2000). More precisely, several research findings point towards the direction that 1) PTSD prevalence rates are significantly lower in older individuals (Reynolds et al., 2016; de Vries & Olff, 2009), 2) there is a change from the typical PTSD triad (e.g., re-experience, avoidance and heightened sense of threat) to more somatoform health symptoms in older age (Glaesmer et al., 2011; Freitag et al., 2013; Pietrzak et al., 2012), and 3) PTSD symptom severity shows a decline over the life course (Böttche et al., 2012) with more subthreshold PTSD symptoms being experienced in older age (Pietrzak et al., 2012). This has also been discussed and outlined by the critical comment on the need for adaptation of age-appropriate diagnostic criteria for PTSD published during the work of this thesis (Maercker, 2021). Yet, older individual's health and well-being may still be notably strained by PTSD symptom representation in older age and hence, it is imperative to examine the impact of trauma exposure and probable PTSD symptoms that persist into older age.

2.2.2 Cognitive Functioning Following the Exposure to Child Maltreatment

As outlined in the previous section, there exists mounting evidence for an association between exposure to child maltreatment and mental health conditions such as PTSD. Yet, the association between child maltreatment and subsequent health alterations is by no means exhaustive by investigating only alterations in the single domain of mental health. As such ample evidence suggests a link between exposure to child maltreatment and alterations in cognitive functioning.

The review by Short and Baram (2019) investigates the relationship between the exposure. To early-life adversity (i.e., low socioeconomic status, war, and child maltreatment) and neurological disease, including cognitive impairment. They concluded that a threefold of factors (i.e., genetic, environmental, and experiential) may be associated with an increased risk for the development of neuro-cognitive impairments following the exposure to early-life adversity, with particular emphasis on the exposure to environmental (e.g., living in poverty, exposure to traumatic events) and experiential (e.g., parental sensitivity, maternal depression, absence of father) factors influencing the brain's maturation when experienced during sensitive developmental periods. More precisely, in the absence of supportive environmental conditions, the developing brain may adopt structural and functional abnormalities which later could express as neurocognitive impairments (Short & Baram, 2019).

This is further in line with results of a recent meta-analysis. Wang and colleagues (2019) report that during childhood and/or adolescence individuals can develop a cognitive reserve capability that can moderate the manifestation of cognitive impairment in older age. However, factors such as the exposure to child maltreatment might impede this development and hence might indirectly affect cognition in older age (Wang et al., 2019). Additionally, the type of exposure to child maltreatment has been found to be a factor to influence cognition in older age. In another study with elderly individuals, Wang and colleagues (2016) observed that

the exposure to neglect during childhood and/or adolescence was associated with mild cognitive impairment in older age (Wang et al., 2016).

As outlined above, most previous research has examined the potential link between exposure to child maltreatment and neuro-cognitive conditions (i.e., mild cognitive impairment). However, given that more and more individuals reach older age stages (Fuster, 2017) and the fact that aging is naturally associated with a decline in cognitive functioning (Harada et al., 2013), there is a need to understand how factors such as child maltreatment affect cognitive functioning in aged individuals. Furthermore, so far there exists only ample evidence for the association between exposure to severe forms child maltreatment in individuals with a history of child welfare care and cognitive health in later life (Burri et al., 2013). As a consensus, there is as gap in the field for the thorough examination of the relationship between the exposure to child maltreatment in welfare care with global levels of cognitive functioning in older age by comparing aged individuals with a history of institutional upbringing versus matched controls.

2.2.3 Physical Functioning Following the Exposure to Child Maltreatment

In addition to cognitive alterations, previous research has identified impairment of physical functioning to be associated with the exposure to child maltreatment (Alastalo et al., 2013; Archer et al., 2017; Greenfield & Marks, 2009). While physical impairment in the form of injuries and malnutrition following physical abuse and neglect may be immediately obvious, a few researchers suggest that the exposure to child maltreatment can also more globally serve as an antecedent of physical impairments throughout the lifespan. More precisely, Greenfield and Marks (2009) reported that individuals with a history of physical or psychological violence in childhood reported higher impairment in various activities (e.g., carrying groceries, walking several blocks, climbing a flight of stairs) as compared to individuals with no such history.

Likewise, in a prospective birth cohort study it was shown that the exposure to neglect, sexual abuse, or psychological abuse during childhood was associated with poor physical functioning at the age of 50 years (Archer et al., 2017). Furthermore, within the same study the authors observed that the likelihood of a decline in physical functioning in adulthood increased by means of experiencing multiple types of maltreatment as a child.

Regarding physical functioning in individuals with a history of child welfare care practices, previous research has focused on examining physical health conditions rather than subjective reports of physical functioning in later life. For instance, in Irish institutional abuse survivors a direct effect of exposure to child maltreatment on physical health (e.g., frequent illness, pain, hospitalization) was observed (Carr et al., 2019). However, the natural aging process is oftentimes associated with a decreased capacity in physical functioning and child maltreatment can serve as an antecedent of decline in physical functioning (Archer et al., 2017). This demonstrates a need to differentiate the loss of physical functioning in the normal aging process compared to that which occurs in aged survivors of child welfare care.

Alongside the previously described studies, a summary of key findings on the association between the exposure to child maltreatment within several welfare care settings and mental, cognitive, and physical health problems in later life is provided in the Table 1.

Table 1

Quantitative Findings on Mental, Cognitive, and Physical Health Associates Following the Exposure to Child Maltreatment in Adult Survivors of Child Welfare Care

Category Author	Date	Type of study	Key Findings
Burri, Maercker, Krammer, & Simmen-Janevska	2013	$N = 96$, $M_{age} = 78$ years, 57 % male	– Within the entire sample higher rates of depressive symptoms as compared to the general population. – Participants with PTSD (22.9%) showed poorer cognitive functioning compared to individuals without PTSD, this was exaggerated in individuals with a history of childhood trauma.
Carr, Duff, & Craddock	2020	$n = 3{,}856$ survivors of institutional abuse and $n = 1{,}577$ controls, $M_{age} = 54$ years, 61% male	– Review revealed an association between history of institutional abuse and poor adjustment in mental health (26% - 88%) and physical health (6% - 74%).
Carr, Nearchou, Duff, Mhaoileoin, Cullen, O'Dowd, & Battigelli	2019	$N = 225$, $M_{age} = 58$ years, 24% male	– Survivors of institutional abuse reported negative outcomes in the domains of psychosocial adjustment (96%), mental health (84%), and physical health (43%).
Carr	2009	$N = 247$, $M_{age} = 60$ years, 55% male	– Around 80% of the participants fulfilled criteria for an anxiety, mood, alcohol or substance use, or personality disorder during their life course.

Jackson, O'Brien, & Pecora	2011	N = 708, age range = 20 - 51 years, 51 % male	–	A total of 20% of the sample reported past year PTSD.
Krammer, Kleim, Simmen-Janevska, & Maercker	2016	N = 116, M_{age} = 77 years, 59% male	–	Exposure to childhood trauma was associated with classic rather than complex PTSD symptoms.
Kuhlman, Maercker, Bachem, Simmen, & Burri	2013	N = 141, M_{age} = 77 years, 59% male	–	Exposure to childhood trauma was associated with geriatric depression symptoms (23% above clinical cut-off), particularly exacerbated following the exposure to emotional abuse.
Lueger-Schuster, Knefel, Glück, Jagsch, Kantor, & Weindl	2018	N = 454, n = 220 survivors of institutional abuse, M_{age} = 58 years, 60% male; comparison group n = 234, M_{age} = 58 years, 35% male	–	Survivors of institutional abuse reported higher prevalence rates in nearly all investigated mental disorder compared to control participants and higher symptom distress.
Salazar, Keller, & Courtney	2011	N = 513, M_{age} = 17 years, 45% male	–	Maltreatment experiences (both precare and during-care) were associated with more depressive symptoms.
Sigal, Rossignol, & Oumet	2003	N = 40, M_{age} =57 years, 100% male	–	Individuals with a history of institutionalization reported more psychosocially dysfunctional and more chronic illnesses (depression, allergies, joint problems, serious back problems). Depression in the male

				group of individuals with a history of institutionalization 12.5% and in the comparison group 2.5%.
Thoma, Bernays, Eising, Pfluger, & Rohner*	2021	*N* = 257, institutional group *n* = 132, M_{age} = 71 years, 58 % male; control group *n* = 125, M_{age} = 71 years, 49 % male	–	The institutional group reported more physical illness, health symptoms, stress, and lower well-being, compared to individuals of the control group.
Thoma, Bernays, Eising, Maercker, & Rohner*	2021	*N* = 257, institutional group *n* = 132, M_{age} = 71 years, 58 % male; control group *n* = 125, M_{age} = 71 years, 49 % male	–	The institutional group reported higher prevalence rates in anxiety disorders, PTSD, somatic disorders, smoking, and psychotic symptoms compared to the control group.
Wolfe, Francis, & Straatman	2006	*N* = 76 , M_{age} = 39 years, 100% male	–	Survivors of abuse of religiously affiliated institution reported current PTSD (42%), alcohol problems (21%), and mood-related disorders (25%).

Note. N/*n* = number of individuals, M_{age} = mean age in years, PTSD = post-traumatic stress disorder;

*Research studies used the sample as subject to Manuscript 1 and Manuscript 2.

2.3 Factors Influencing Health Following the Exposure to Child Maltreatment

When investigating and aiming to explain the association between exposure to child maltreatment and alterations in health, previous research has identified significant inter-individual variation in the domains of mental, cognitive, and physical health (Bonanno, 2004; Burri et al., 2013; Schafer et al., 2014). Hence it is argued that mediators might influence the association between exposure to child maltreatment and health in later life (Shenk et al., 2014). The following section introduces two factors and their theoretical concepts on how mental, cognitive, and physical health might be influenced following the exposure to child maltreatment. First, two theoretical models will be introduced; the *theory of cumulative advantage/disadvantage* and the *stress sensitivity hypothesis*, that aim to explain the accumulation of stressful life events and heightened reactivity towards future stressors, following the exposure to child maltreatment. Next, the impact of social acknowledgement experienced as a victim or survivor following the exposure to potentially traumatic events and its potential long-term associates for mental health will be described.

2.3.1 Stressful Life Events: Cumulative Disadvantage and Stress-Sensitivity

An attempt to explain inter-individual variation following the exposure to child maltreatment stems from the belief that early exposure to child maltreatment may result in cumulative or even chronic psychological stress, which indirectly influences health over the life course (Scott-Storey, 2011). In fact, in previous studies it has been observed that adult survivors of child maltreatment reported heighted rates of exposure to life stressors (Widom, et al., 2008). Of particular interest for the present thesis, this heightened level of exposure to future stressful events has also been described in survivors of institutional abuse (Lueger-Schuster et al., 2018). The theory of cumulative disadvantage (Dannefer, 2003) and the stress sensitivity hypothesis

(Harkness et al., 2015), described below, aim to explain this long-term accumulation of stress exposure.

2.3.1.1 Cumulative Disadvantage

Numerous research findings propose that a single type of abuse or neglect during childhood and/or adolescence is rarely experienced in isolation, but that multiple forms of child maltreatment (e.g., physical abuse, physical neglect, emotional abuse, emotional neglect) co-occur (Kessler et al. 2010). Similar to the previously described dose-response relationship between the exposure to child maltreatment and heightened risk to be affected by various health factors (see *Health Associates Following the Exposure to Child Maltreatment*), there exists empirical evidence that following the exposure to child maltreatment an individual subsequently experiences more highly stressful life events (e.g., revictimization, adverse adult events, serious accidents) (Desai et al., 2002; LaNoue et al., 2012; Widom et al., 2008). The *theory of cumulative advantage/disadvantage* (Dannefer, 2003) and the *cumulative inequality theory* (Ferraro & Shippee, 2009) propose a theoretical framework aiming to explain this accumulation of disadvantage and inequality over the life course. According to Dannefer (2003) cumulative advantage/disadvantage can be defined as the „systematic tendency for interindividual divergence in a given characteristic (e.g., money, health, status) with the passage of time" (p. 327).

Even though this concept was originally developed in the context of sociology (Maddox & Douglass, 1974) - examining structural basic forces that lead to early disadvantage and result in subsequent experienced disadvantage - there is much to suggest that this conceptualization might also ameliorate present understanding on developmental trajectories following the exposure to child maltreatment. As such, several studies have reported findings that individuals

who have been exposed to child maltreatment are more prone to experience additional stressful life events in its aftermath (LaNoue et al., 2012; Patwardhan et al., 2017).

This accumulation of life stressors has further been observed in individuals with a history of child welfare care. From pertinent studies, it has been shown that individuals with a history of child welfare care were prone to start off with a lower socio-economic status (Thoma et al., 2021b), poor academic achievements (MacLean, 2003), and severe, frequent, and protracted exposure to child maltreatment (Carr et al., 2020b), and thereafter showed increased odds to be exposed to a higher number of stressful events throughout their lives (Carr et al., 2019; Lueger-Schuster et al., 2018).

Furthermore, this accumulation of life stressors and inequalities is thought to act as a chronic stressor, leading to changes within the body (e.g., allostatic load) (McEwen, 2004) and thereupon increasing the susceptibility to future life stressors, referred to as stress sensitivity (Hammen et al., 2000). The hypothesis of stress-sensitivity is explained in more detail in the following section.

2.3.1.2 Stress Sensitivity

Originally stemming from research studies with chronically depressed patients, it is argued that heightened levels of early stress exposure create a state of vulnerability that makes the individual more prone to subsequent increased levels of stress exposure– conceptualized in the stress sensitivity hypothesis (Hammen et al., 2000). In more detail, the hypothesis posits those individuals experiencing repeated or chronic exposure to psychological stress (i.e., affective episodes) become highly sensitive to subsequent stress, so that the exposure to comparably minor stressors leads to excessive stress responses and increases the susceptibility for future depressive episodes (Harkness et al., 2015; Monroe & Harkness, 2005). The literature also shows that this repeated and chronic exposure to psychological stress can lead to potentially

long-lasting alterations within the human organism (McEwen, 2002). These changes may thereupon increase the risk for several health conditions years after the initial exposure to child maltreatment has ended (Kendall-Tackett, 2002). Furthermore, from pertinent studies it is revealed that, in particular, a history of interpersonal violence is associated with subsequent potentially traumatic events (Benjet et al., 2016). The high rates of exposure to early interpersonal life adversity within several child welfare care cohorts suggests that this might also be the case for today's survivor populations (Wolfe et al., 2003; Burri et al., 2013; Lueger-Schuster et al., 2018). Indeed, within the previously introduced Austrian sample, rates of exposure to adult life events were particularly pronounced in individuals with a history of child welfare care (Lueger-Schuster et al., 2018).

2.3.2 The Socio-Interpersonal Model: Social Acknowledgement and Post-Traumatic Stress Response

As the diagnosis of PTSD is based on the exposure to an external potentially traumatic event, there is much to suggest that environmental factors need to be considered when investigating post-traumatic stress responses (Bonnan-White et al., 2018). The socio-interpersonal model conceptualized by Maercker and Horn (2013) takes into account the perceived individual influences of family members, peers, and the society following the exposure to a potentially traumatic event. In more detail, the model posits the importance of three levels. The first level comprises individual social affective responses such as shame, guilt, anger, and revenge. On the second level the model positions close relationships in which disclosure, social support, and/or negative exchange play an important role. On the third level is the distant social context that comprises aspects of the culture and society like the collective experience of trauma, social acknowledgment as victim or survivor, and a given cultural value orientation (Maercker &

Horn, 2013; Maercker & Hecker, 2016) (see Figure 1 for a graphical representation of the socio-interpersonal model).

Of relevance for the present thesis and central to the socio-interpersonal model is the construct of social acknowledgement (Maercker & Mueller, 2004). Social acknowledgement refers to the degree an individual feels understood and supported by their social environment; Do people show sympathy following the exposure of the potentially traumatic event? Can the individual disclose their experiences in front of their family and friends? Does the individual feel underestimated or overprotected by his or her social environment? Several research studies have examined the potential beneficial as well as exacerbating effects of low and high levels of social acknowledgement following trauma exposure. In more detail, it has been shown that low levels of social acknowledgement following the exposure to a potentially traumatic event were associated with high levels of PTSD symptoms as well as PTSD severity (Jones et al., 2006; Maercker & Mueller, 2004; Mueller et al., 2009) whereas higher levels of social acknowledgement were associated with lower levels of post-traumatic cognitions and PTSD symptoms (Jones et al., 2006; Mueller et al., 2008; Xu et al., 2016). Altogether these findings suggest that the individual is highly sensitive on how their social network and the society respond following his or her exposure to potentially traumatic events.

Social acknowledgement might also be an important construct for today's aged survivors with a history of welfare care. Previously it has been suggested that social constructs have a particularly important role among well-being in older age (Antonucci & Akiyama, 1987; Fiori et al., 2007). Furthermore, the reappraisal movement of child maltreatment across several child welfare care settings has just been brought forward within recent years. Accordingly, one could argue that the societal and environmental response to the severe forms of child maltreatment within these settings was far from supportive and empathetic. This is in line with survivor testimonies in which they have felt powerless, stigmatized, and left alone with their

experiences (Page & Clark, 1977). The Zeitgeist at the time largely saw minors in care settings as 'orphans' and 'criminals', which in turn promoted societal stigmatization (Page & Clark, 1977; Stein 1983). In settings where individuals were provided with the ability to disclose their experiences, perceived social support, and understanding from their environment, PTSD symptom manifestation was observed to be lower (Carr et al., 2020b). Hence there is much to suggest that perceived levels of social acknowledgement profoundly shaped post-traumatic stress responses in individuals with a history of institutional upbringing.

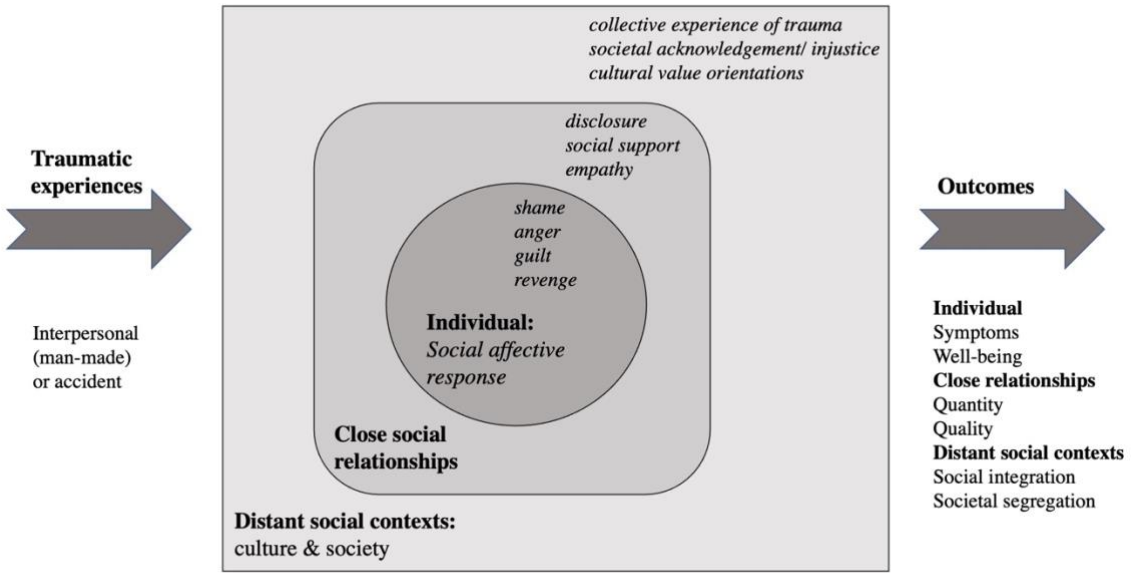

Figure 1. The socio-interpersonal model as a theoretical framework following the exposure to potentially traumatic events (Adapted from: Maercker & Horn, 2013; Maercker & Hecker, 2016).

2.4 Neurobiological Underpinnings of Aging, Exposure to Potentially Traumatic Events and Probable Post-Traumatic Stress Disorders Symptoms

During the last century, neuroimaging techniques have become a critical tool in identifying and studying the brain's structure and function by means of magnetic resonance imaging (Insel, 2011). Functional magnetic resonance imaging (fMRI) measures brain activity (e.g., functional connectivity) by picking up signal fluctuations that reflect underlying changes in blood, oxygenation, and flow, stemming from variations in neural metabolic demands (Logothetis, 2002). As such, resting-state functional magnetic resonance imaging (rs-fMRI), occurring in the absence of task demands, is used to study intrinsic connectivity patterns by measuring spontaneous signal fluctuation over time and has become a dominant technique due to noninvasivness and relative ease to conduct (Biswal, 2012).

Moreover, within recent years, particular interest has focused on the investigation of alterations in resting-state functional connectivity (rs-FC) associated with aging. As such, it has been established that FC within networks decreases with age while connectivity between networks increases, which is referred to as functional dedifferentiation (Chan et al., 2014; Geerligs et al., 2015; Malagurski et al., 2020; Song et al, 2014; Zonneveld et al., 2019). Previous studies have however observed great variability regarding rs-FC in older age and have suggested that additional factors over the life course need to be taken into consideration to explain the heterogeneity in the brain's organization in older age (Jockwitz & Caspers, 2021; Zonneveld et al., 2019). One factor that is suggested to profoundly influence rs-FC is the exposure to potentially traumatic events and the development of PTSD symptoms (Bluhm et al., 2009; DiGangi et al., 2016; Kunimatsu et al., 2020; Sheynin et al., 2020). The following section will first discuss the literature regarding rs-FC in association with aging and then outline the relationship between rs-FC and the exposure to a potentially traumatic event and probable PTSD symptoms.

2.4.1 Functional Connectivity and Aging

With the increasing numbers of individuals reaching older ages, today's society is experiencing a shift towards a profoundly aged population (Fuster et al., 2017). With this, demands for tailored health care services specifically addressing health in aging relevant domains is of particular interest. To provide the best possible care, there is the need to understand factors that influence healthy aging. Based on current literature, it is known that the brain's structure and FC are affected by aging and associated neurogenerative diseases (Peters, 2006; Rossini et al., 2007; Wu et al., 2013). In a similar vein, changes in FC in the aging brain particularly in neurodegenerative conditions (e.g., Alzheimer's disease) have become a popular domain of investigation (Dennis & Thompson, 2014; Lin et al., 2018). Nevertheless, also the 'normal' aging brain has been shown to display critical changes in FC (Damoiseaux, 2017; Malagurski et al., 2020; Wig, 2017) and ample evidence suggests that functional changes might even precede structural alterations in aging (Jack et al., 2010; Zonneveld et al., 2019).

Alterations in FC can be categorized as functional segregation and/or functional integration. Functional segregation refers to clustered connectivity of highly interconnected modules, whereas connectivity between modules of different clusters is termed functional integration (Damoiseaux, 2017; Tononi et al., 1994). With regards to aging, it is established that FC within networks decreases (i.e., less functional segregation) with age while connectivity between networks increases (i.e., more functional integration) - termed as functional dedifferentiation (Chan et al., 2014; Ferreira et al., 2016; Malagurski et al., 2020). However, so far, most research examining functional dedifferentiation in aging has been conducted using cross-sectional data (Chan et al., 2014; Damoiseaux, 2017) and only a few studies have been able to confirm these findings with longitudinal data repositories (Ng et al., 2016; Malagurski et al., 2020). However, to confirm intra-individual changes associated with aging, further longitudinal investigations across different aging cohorts are needed, including

higher resolution of specific age brackets (e.g., 70-74, 75-79, etc.) or even the consideration of age as a continuous variable (Garfein & Herzog, 1995). Furthermore, given the fact that previous observations of the brain's intrinsic organization in older age have shown great heterogeneity across individuals (Jockwitz & Caspers, 2021; Zonneveld et al., 2019), it is vital to study additional factors that are associated with functional changes over the life course. The next section describes rs-FC findings following trauma exposure and PTSD symptoms.

2.4.2 Factors Influencing Functional Connectivity in Older Age: Exposure to Potentially Traumatic Events and Probable Post-Traumatic Stress Disorder Symptoms

Previous neuroimaging studies have revealed differences with respect to FC between and within intrinsic connectivity networks (ICNs) in individuals with probable PTSD, trauma-exposed individuals without PTSD, and non-trauma exposed individuals (Sheynin et al., 2020; Sripada et al., 2012). Moreover, pertinent studies revealed the importance of two ICNs: a) the default mode network (DMN), known to be active during internally directed thoughts and cognition (e.g., mind wandering) (Buckner et al., 2019), and b) the salience network (SN), implicated in detecting and evaluating external stimuli (Uddin, 2015).

For instance, a study of individuals with chronic PTSD resulting from early life trauma compared to healthy controls showed that resting state low-frequency activity in the posterior cingulate cortex/precuneus (i.e., areas of the DMN) was less strongly correlated with activity in other areas of the DMN for individuals with chronic PTSD (Bluhm et al., 2009). Furthermore, in a recent rs-FC study of adolescents with PTSD, asymptomatic controls and trauma-exposed controls, only participants with PTSD had reduced connectivity within DMN compared to asymptomatic controls and trauma-exposed controls (Sheynin et al., 2020).

Additionally, the SN has been found to show aberrant functional connectivity in individuals with PTSD. For instance, a study of returned veterans with PTSD, veterans without

PTSD, and community controls, showed increased connectivity within the SN in veterans with PTSD (Sripada et al., 2012). Nevertheless, there have been mixed results regarding the specificity of aberrant SN connectivity in association with PTSD symptoms. For example, not all previous studies detected differences in within-SN connectivity when comparing individuals with PTSD to trauma-exposed individuals without PTSD symptoms (Sheynin et al., 2018). However, not all previous studies compared a threefold group differentiation (e.g., individuals with PTSD, trauma-exposed individuals without PTSD and individuals without trauma exposure), which might be crucial when investigating SN connectivity in association with PTSD symptoms (Abdallah et al., 2019; Sripada et al., 2012). In the same vein, Sheynin and colleagues (2020) argue that greater within SN-connectivity can also be detected when comparing trauma-exposed individuals with non-trauma exposed individuals, suggesting that it may be the exposure to potentially traumatic events alone that contributes to a differential involvement of several brain regions of the SN (e.g., right anterior insula, basal ganglia) (Stark et al., 2015).

Additionally, it has been shown that individuals with PTSD also exhibit greater cross-network FC between DMN and SN in comparison to non-trauma exposed individuals (Block et al., 2017; Zhang et al., 2015). In fact, Sheynin and colleagues (2020) observed greater DMN-SN connectivity in individuals with PTSD compared to trauma-exposed individuals without PTSD, but not to individuals who had not experienced potentially traumatic events. Hence, one might suggest that alterations in DMN-SN connectivity, indicative of reduced segregation between these networks, are associated with probable PTSD symptom expression and occur independently of the exposure to potentially traumatic events. Hence the proposed threefold differentiation might also be crucial when investigating the DMN-SN connectivity following trauma exposure and in association with probable PTSD symptoms.

Furthermore, as outlined above (see *Post-Traumatic Stress Disorder Following the Exposure to Child Maltreatment*), PTSD symptom expression is thought to change throughout the life course with lower PTSD prevalence rates, more somatoform symptoms, a decline in PTSD symptom severity and more subthreshold PTSD symptoms in older age (Averill & Beck, 2000). Yet, given the fact that an increasing number of individuals reach older age stages (Fuster, 2017) and that their health and well-being may still be remarkably strained by the PTSD symptom representation in older age (Pietrzak et al., 2012), it is imperative to examine the impact of exposure to potentially traumatic events and in association with probable PTSD symptoms on the brain's FC in older non-clinical samples (i.e., non-treatment seeking older adults).

3 THE PRESENT THESIS

The overarching aim of the present thesis is to examine mental, cognitive, physical, and neurobiological health following the exposure to potentially traumatic events with a particular focus on the effect of childhood maltreatment in older age.

Three main research questions were formulated:

1. What are older age health associates in the domains of mental, cognitive, and physical functioning following the exposure to child maltreatment and within the context of child welfare care?
2. Which factors following the exposure to child maltreatment influence health associates in the domains of mental, cognitive, and physical functioning over the life course until older age?
3. What are neural underpinnings using rs-fMRI connectivity following the exposure to potentially traumatic events and in association with probable PTSD symptoms in older age?

The next chapter will outline the two projects underlying this thesis, followed by a chapter summarizing the main findings of the three manuscripts and a chapter discussing their implications. The full-length manuscripts are provided within the last chapter.

3.1 Project Overview

The present thesis integrated two projects focused on the effect of exposure to potentially traumatic events and child maltreatment on the domains of mental, cognitive, physical, and neurobiological health in older age individuals, and was organized and conducted at the University Zürich, as described in the following sections.

3.1.1 National Research Program 76: Welfare and Coercion

The first two manuscripts (Manuscript 1 and Manuscript 2) are part of the National Research Program (NRP76) 'Welfare and Coercion – Past, Present and Future' founded by the Swiss National Science Foundation (SNF) with the aim of investigating the nature as well as the consequences of Swiss welfare practices as performed in Switzerland until 1981. In more depth, the sample underlying Manuscript 1 and Manuscript 2 is drawn from Project Thoma, an ongoing research project with the title '*Differential Aging Trajectories in High-Risk Individuals with Past Experiences of Early Adversity'*. While the Project Thoma is a prospective longitudinal study, data for the presented manuscripts stems from the baseline assessment conducted between July and December 2019. The project is registered with the grant number 407640_177355/1 and was approved by the Ethics Committee of the Faculty of Art and Social Sciences in the University of Zürich (ID: 19.4.3). Manuscript 1 focuses on the examination of lifetime PTSD following the exposure to child maltreatment by investigating elements of the child maltreatment (e.g., severity, variety, type) and following child maltreatment (e.g., stressful life events, social acknowledgement) in a group of individuals with a history of child welfare care and an age matched control group (Eising, Voelkle, Rohner, Maercker, & Thoma, 2021). Manuscript 2 assess cognitive and physical functioning following the exposure to child maltreatment and in association with a history of child welfare care and

further examines the potential mediating effect of life stressors on functioning in older age (Eising, Thoma, Voelkle, Pfluger, Maercker, & Rohner, 2021).

3.1.2 Longitudinal Healthy Aging Brain Database Project

The third manuscript belongs to a prospective longitudinal study *'The Longitudinal Healthy Aging Brain Database Project (LHAB)'*(Zöllig et al., 2011). The aim of the project is to investigate longitudinal changes in brain structure, function and their behavioral correlates in subjects aged 65 years and older. Data acquisition started in 2011 and has since been conducted at the International Normal Aging and Plasticity Imaging Center (INAPIC) at the University of Zürich. By means of rs-fMRI, Manuscript 3 examines and compares differences in within- and between-network rs-FC between trauma-exposed individuals with and without probable PTSD symptoms as well as non-trauma exposed individuals (Eising, Maercker, Malagurski, Jäncke, & Mérillat, 2021). The aim was to investigate whether within- and between-network rs-FC in the DMN and SN change across time as a function of aging, the exposure to potentially traumatic events, and in association with probable PTSD symptoms. The project was supported by the Velux Stiftung (project No. 369), the Swiss National Science Foundation (grant 100014-122613/1) and the University Research Priority Program "Dynamics of Healthy Aging" of the University of Zürich.

3.2 Summary of Manuscript 1: Lifetime Post-traumatic Stress Disorder in Older Individuals with a History of Institutional Upbringing in Childhood: The Role of Social Acknowledgement and Stressful Life Events

Aim: Child maltreatment experiences are known to increase the risk of developing mental health disorders, including post-traumatic stress disorder (PTSD). Previous research has shown that contextual factors during child maltreatment, such as duration, severity, type and social setting, and the context subsequent to child maltreatment such as perceived levels of social acknowledgement and stressful life events, have a meaningful impact on the link between child maltreatment and PTSD. From pertinent studies it has become clear that many aged survivors with a history of institutional upbringing were subject to severe levels of exposure to child maltreatment. Given that most previous studies have focused on young to middle-aged adults, combined with the current global demographic shift towards an aging society, there is a critical need for an investigation of the elements contributing to PTSD in aged survivors of institutional upbringing.

Methods: The analysis underlying Manuscript 1 was based on data from $N = 238$ Swiss older adults (mean age = 70.50 years, 47% female), with $n = 116$ individuals with a history of institutional upbringing (mean age = 70.25, 41% female) and $n = 122$ individuals of the control group (mean age = 70.71 years, 51% female). Data was derived from a structured clinical interview, standardized questionnaires assessing child maltreatment, stressful life events and social acknowledgment. Regression and mediation analyses were performed to examine associations between child maltreatment, stressful life events and lifetime PTSD as well as to examine the potential mediating role of social acknowledgement between child maltreatment and lifetime PTSD.

Results: Results showed that individuals with a history of institutional upbringing reported higher levels of exposure to child maltreatment and more lifetime PTSD in older age as compared to individuals without such history. Level of exposure to child maltreatment, but not necessarily a history of institutional upbringing, was related to higher lifetime PTSD and more stressful life events over the life course. For individuals of the control group, the association between child maltreatment and lifetime PTSD was mediated by social acknowledgement.

Discussion: Results from Manuscript 1 provide support for heightened PTSD prevalence in older individuals with a history of institutional upbringing and call for specific treatment approaches within the at-risk population. Furthermore, individuals with high levels of exposure to child maltreatment are more prone for low social acknowledgment and potential future traumatization in form of stressful life events. Hence, therapeutic interventions might benefit from incorporating social interpersonal skills training to enhance well-being into older age.

3.3 Summary of Manuscript 2: Cognitive and Physical Functioning in Older Adults with a History of Child Welfare Care: Investigating the Mediating Role of Life Stressors

Aim: Although child maltreatment has repeatedly been linked to negative health implications, most research has focused on examining the association between child maltreatment and mental health. Furthermore, comparably few investigations have probed the association of exposure to child maltreatment in aging-relevant health domains such as cognitive and physical functioning. When examining long-term associates following the exposure to child maltreatment, an emerging study group of interest are individuals with a history of child welfare care, given their increased risk to having been exposed to severe forms of child maltreatment within these settings. The present study aimed to investigate long-term associates of exposure to child maltreatment, and specifically in the context of welfare care, in form of cognitive and physical functioning in older age, as well as to study the potential mediating role of life stressors of this relationship.

Methods: A total of $N = 253$ participants were assessed of which $n = 130$ had been subjected to child welfare-care (welfare care group, mean age = 70.82, 42% female) and $n = 123$ age-matched controls (mean age = 70.74, 50% female). A battery of standardized instruments (e.g., self-report inventories and behavioural assessments) were used to assess exposure to child maltreatment, life stressors, cognitive and physical functioning. To answer the research questions, analyses included regression, mediation analysis and a MANCOVA.

Results: The level of exposure to child maltreatment was not associated with lower levels of cognitive functioning but was linked to lower levels of physical functioning in older age. The group contrast revealed that individuals with a history of child welfare care showed lower cognitive and physical functioning in comparison to the age-matched control group. Life

stressors mediated the relationship between exposure to child maltreatment and subjective physical functioning in the welfare care group.

Discussion: Results of Manuscript 2 suggested that exposure to child maltreatment is associated with lower physical functioning in older age and a history of child welfare care additionally is associated with lower cognitive functioning in aged individuals. In the welfare care group, the association between exposure to child maltreatment and physical functioning was further mediated by high rates of exposure to life stressors, demonstrating the increased risk for being exposed to life stressors over the life course in this group. Based on present findings, there is much to suggest that policymakers should direct attention and resources towards the prevention of exposure to child maltreatment and the treatment of affected individuals, to counteract the associated long-term implications in aging-relevant domains.

3.4 Summary of Manuscript 3: A Longitudinal Resting-State Functional Connectivity Analysis on Trauma Exposure and Post-traumatic Stress Symptoms in Older Individuals

Aim: Neuroimaging studies have revealed interindividual differences in the brain's functional connectivity associated with aging. Differences in functional connectivity have further been observed in individuals following the exposure to potentially traumatic events and in association with probable PTSD symptoms. The question of neurobiological variability in individuals with prior trauma exposure and probable PTSD symptoms is furthermore relevant in the context of aging, given the present demographic shift towards an aging society. The aim of the third study was to investigate differences in with-DMN, within-SN and between DMN-SN rs-FC between trauma-exposed individuals with and without PTSD symptoms as well as non-trauma exposed individuals in a non-clinical older adult sample (> 65 years).

Methods: Resting-state fMRI and behavioral data stem from the Longitudinal Healthy Aging Brain Database Project (LHAB) conducted at the University of Zürich. A total of $N = 110$ participants (mean age = 70.55 years, 50% female), who completed the questionnaires on trauma exposure and post-traumatic stress symptoms were included.

Results: The presence of PTSD symptoms was associated (trend-level) with lower within-DMN connectivity relative to trauma-exposed individuals without PTSD symptoms. Trauma-exposure itself was found to be associated (trend-level) with higher within-SN connectivity compared to rs-FC to non-trauma exposed individuals. The rs-FC between the DMN-SN was increased across time as consistent with previous models of healthy aging.

Discussion: Results of Manuscript 3 identified that alterations in within-DMN and within-SN rs-FC also occur in non-treatment seeking older adult populations following the exposure to

potentially traumatic events and in association with PTSD symptoms and manifest in addition to DMN-SN rs-FC in older age.

4 GENERAL DISCUSSION

In Chapter 4 an overall discussion of the results as well as a contextualization of relevant background information of the present thesis are provided. First, the results obtained in Manuscript 1 and Manuscript 2 are discussed and integrated with current literature. Second, findings of Manuscript 3 are evaluated and discussed by integrating the results obtained in Manuscript 1 and Manuscript 2. Aspects that have already been addressed and discussed within the three manuscripts will not be discussed in detail again, but are provided at the end of the thesis in the full length manuscripts (see Chapter 5). Thereafter limitations of the present thesis will be addressed followed by a discussion of future directions for this research, clinical implications, and policy and practice. The end of this chapter closes with a general conclusion.

4.1 Empirical Evidence for Mental, Cognitive, Physical, and Neurobiological Health Following the Exposure to Potentially Traumatic Events

The overall objective of this thesis was to investigate health associates following the exposure to potentially traumatic events with a focus on associates of child maltreatment that persist into older age. To address these aims, Manuscript 1 and Manuscript 2 investigate how mental, cognitive, and physical functioning following the exposure to child maltreatment, and within the context of child welfare care, manifest over the life course (i.e., lifetime PTSD) and until older age (i.e., cognitive, and physical functioning in older age). Additionally, the first two manuscripts examined factors that occurred after the exposure to child maltreatment in older individuals by investigating subsequent life stressors and the individual's perception of social acknowledgement following the exposure to potentially traumatic events. Within the third manuscript, neural underpinnings following the exposure to potentially traumatic events and in association with probable PTSD symptoms were investigated by means of rs-fMRI in a non-clinical older adult sample.

4.1.1 Health Associates Following the Exposure to Child Maltreatment: Post-Traumatic Stress Disorder, Cognitive, and Physical Functioning

Results of the first study (Manuscript 1) showed that across groups (e.g., older adults with a history of institutional upbringing vs. no history of institutional upbringing), individuals with higher levels of exposure to child maltreatment reported higher levels of lifetime PTSD symptomatology. When controlling between groups, a secondary analysis revealed that the driving factor for lifetime PTSD was the total exposure to child maltreatment, regardless of whether it occurred in an institutional setting.

Results of the second study (Manuscript 2) revealed that the level of exposure to child maltreatment was significantly associated with the level of physical functioning in older age but not with the level of cognitive functioning across groups. More precisely significant inverse associations were found between the exposure to child emotional neglect, physical and sexual abuse, and subjective physical functioning in older age. In contrast with lifetime PTSD symptomatology (Manuscript 1), comparisons between groups revealed that individuals with a history of institutional upbringing reported worse outcomes on all four measures of cognitive and physical functioning compared to individuals without a history of institutional upbringing.

Building on present findings, it can be tentatively concluded that lifetime PTSD symptomatology shows a strong association with level of exposure to child maltreatment whereas level of physical and cognitive functioning in older age are particularly impaired in individuals with a history of institutional upbringing, who had a higher risk of being affected by severe and frequent exposure to child maltreatment.

Moreover, results of Manuscript 1 and Manuscript 2 suggest that individuals placed into institutional settings were prone to experience a triad of risk factors and intermingled events over their life course. First, by means of placing minors into welfare care settings, the individual was prone to experience severe forms of exposure to child maltreatment. Second,

the exposure to severe levels of child maltreatment was found to be associated with an increased risk for developing lifetime PTSD symptomatology and exposure to subsequent life stressors. Third, the placement of minors within institutional settings and the exposure to subsequent life stressors was associated with particularly low levels of physical functioning in older age. In the following section, the second and third risk factors, which expand on previous findings, will be discussed in more detail.

Regarding the second risk factor, it has previously been shown that the exposure to child maltreatment within institutional settings is associated with an increased risk of developing PTSD symptoms (Carr et al., 2020b; Lueger-Schuster et al., 2018). However, the novelty of the current thesis is the finding that lifetime PTSD symptoms were related to the exposure to child maltreatment in a dose-response relationship rather than the placement of a minor within an institutional setting per se. Hence, present results suggest that the manifestation of PTSD symptoms revealed a stronger association with the level of exposure to child maltreatment and not necessarily with the fact of having been brought up in an institutional setting or of having been taken away from their families. However, during the baseline data collection of the NRP76 study no precise differentiation was made between exposure to child maltreatment within the family of origin and within the context of welfare care (i.e., institutional abuse). Therefore, no definite conclusions can be drawn but only a tentative interpretation of the higher significance of the mere exposure to child maltreatment can be provided. Future research studies are warranted to incorporate the differentiation of the context of exposure to child maltreatment as to further present understanding.

Regarding the second risk factor, on a theoretical level, the findings from Manuscript 1 and Manuscript 2 provide support for the theory of cumulative disadvantage and suggest the presence of stress sensitization. More precisely, results of Manuscript 1 revealed that individuals with higher levels of exposure to child maltreatment were also more prone to

experience more stressful life events in comparison to individuals with lower levels of exposure to child maltreatment. However, same as for lifetime PTSD symptomatology, no differences in quantity of exposure to subsequent adult stressful life events (also termed life stressors) were observed between individuals with a history of institutional upbringing as compared to individuals without such history.

Previously, research studies have investigated the theory of cumulative advantage/disadvantage regarding differences in physical functioning based on more general forms of exposure to early-life adversity (e.g., socio-economic status, income, education status). More precisely, differences in socio-economic status and level of education have been reported to increase the gap in self-reported physical functioning in older age (Kim & Richardson, 2011; Mirowsky & Ross, 2005). Similarly, a recently published manuscript using the same data set underlying Manuscript 1 and Manuscript 2 has demonstrated that socio-economic factors mediated the relationship of physical health outcomes and subjective well-being between groups (i.e., those with history of institutional upbringing vs. no history of institutional upbringing), with individuals with a history of institutional upbringing reporting lower levels of education, lower income and lower satisfaction with their financial situation (Thoma et al., 2021b). Results of Manuscript 2 expand on these findings by suggesting that in addition to the detrimental impact of factors such as low socio-economic and education status on cumulative disadvantage, the mere exposure to child maltreatment and life stressors also augments cumulative disadvantage and leads to lower physical functioning in older age.

Furthermore, regarding stress sensitivity, previous literature has revealed a link between exposure to child maltreatment, ongoing chronic stress, and neuroticism (Luo et al., 2021). As neuroticism is associated with a negative evaluation of one's surroundings (Ebstrup et al., 2011), these findings suggest that following the exposure to severe forms of child maltreatment the individual might perceive future potentially traumatic events as more

stressful. Future research is needed to examine whether the mere exposure to potentially traumatic events (cumulative disadvantage) runs in parallel with also a more salient and negative processing of potential confrontation with future potentially traumatic events.

Manuscript 2 expanded on this by exploring the potential role of life stressor as a mediator between exposure to child maltreatment and cognitive and physical functioning in older age – the third risk factor that arises from the placement of minors within institutional settings. Here only for individuals with a history of institutional upbringing, the mediating role of life stressors between exposure to child maltreatment and subjective physical health were observed. That is, individuals with a history of institutional upbringing who reported higher levels of exposure to child maltreatment also reported to have been exposed to more life stressors in adulthood and thereupon indicated worse subjective physical health in older age. Emotional neglect and physical and sexual abuse were found to be particularly associated with lower self-rated physical health, and individuals with a history of institutional upbringing showed lower levels cognitive and physical functioning. These findings suggest that certain types of child maltreatment are more frequently experienced in individuals with a history of institutional upbringing and may be particularly related to decreased cognitive and physical functioning in older age. This is in line with previous findings both internationally and domestically, where individuals with a history of institutional upbringing reported both high rates and severe forms of exposure to emotional neglect (Thoma et al., 2020a), physical and sexual abuse (Lueger-Schuster et al., 2018), and more pronounced physical health problems (Carr et al., 2019, Carr et al., 2020; Sigal et al., 2010; Thoma et al., 2021b) when compared with individuals without such history.

Several contextual factors during institutional upbringing may be associated with the observed high levels of exposure to emotional neglect, physical and sexual abuse. For instance, within welfare care settings minors oftentimes experienced frequent changes of the primary

care giver and due to the Zeitgeist might have experienced severe societal stigmatization (e.g., minors in welfare care systems) (Hill, 2004; Wolfe et al., 2006), making the individual more prone to experience emotional neglect during childhood and/or adolescence. Furthermore, the nature of the care settings – hierarchical structure, power of the institution and disbelief in the minors in care testimonies (Stein, 2006) – facilitated exploitation and brutal mistreatment in form of sexual and physical abuse. Hence, there is much to suggest that several factors specifically experienced within welfare care settings led to the experience of severe emotional neglect as well as physical and sexual abuse in childhood and/or adolescence which in turn are associated with a long-term decrease in cognitive and physical functioning.

Additionally, on a theoretical level, findings of Manuscript 1 provide support for the importance of socio-interpersonal factors on the long-term effects of child maltreatment. Individuals of the control group, who had no history of institutional upbringing, reported higher levels of social acknowledgement than individuals with a history of institutional upbringing, which in turn mediated the relationship between exposure to child maltreatment and lifetime PTSD symptomatology. Similarly, it has been proposed that post-traumatic stress responses are dependent on the judgements of the society, family, and friends as experienced by the individual following the exposure to a potentially traumatic event (Maercker & Mueller, 2004). Given the fact that the disclosure and reappraisal of child maltreatment experienced across child welfare care settings has just been brought forward within recent years, one could argue that the societal response at the time following the severe form of child maltreatment was far from being adequate, which might account for the low levels of perceived social acknowledgment in individuals with a history of institutional upbringing within the present study. This is further supported by reports of survivors who testified to have felt powerless, stigmatized, and left alone with their experiences (Page & Clark, 1977). The Zeitgeist at the time largely saw minors in care settings as ‘orphans’ and ‘criminals’, which in turn aggravated

the perceived societal stigmatization (Page & Clark, 1977; Stein, 1983). Individuals of the control group might have been less affected by societal stigmatization and therefore might have report higher levels of perceived social acknowledgment which could have potentially buffered them from high rates of lifetime PTSD symptom manifestation. An avenue for future research would be to conduct interventions to augment low rates of social acknowledgement in individuals with a history of institutional upbringing with the aim of decreasing potential post-traumatic stress sequalae in affected individuals.

4.1.2 Neurobiological Underpinnings Following the Exposure to Potentially Traumatic Events and Associated with Probable Post-Traumatic Stress Disorder Symptoms

While Manuscript 1 and Manuscript 2 examined mental, cognitive, and physical health associations following the exposure to child maltreatment, Manuscript 3 expanded on this by further investigating neurobiological underpinnings of the exposure to potentially traumatic events and in association with probable PTSD symptoms in older age. The investigation of neurobiological underpinnings in older age is of great relevance given the shift of today's society towards an aging population (Fuster, 2017) and the associated challenge of handling and treating age-related diseases which may be revealed when investigating neural correlates (Lin et al., 2018). Furthermore, the control group in Manuscript 1 and Manuscript 2, who were individuals from the general population with no history of an institutional upbringing, still reported relatively high rates of exposure to child maltreatment and potentially traumatic events over the life course. Therefore, there are grounds for examining the impact of exposure to potentially traumatic events in older adult samples stemming from the general population, as has been done in Manuscript 3. Moreover, older adults may display relatively low prevalence rates of past year PTSD, as it has been shown that subthreshold PTSD is more common in older age, and this population is therefore under-represented or even entirely neglected when only

examining clinical populations (Reynolds et al., 2016; de Vries & Olff, 2009). Hence, the findings of Manuscript 3 contribute to the present state of knowledge of neural underpinnings following the exposure to potentially traumatic events and in association with probable PTSD symptoms in a non-clinical older adult sample.

Furthermore, on a theoretical level, the findings of Manuscript 1 and Manuscript 2 provide support for the theory of cumulative disadvantage and cumulative abuse – early exposure to life stressors leads to cumulative and chronic subsequent stressors and thereby negatively impacts health (Dannefer, 2003; Scott-Storey, 2011). These manuscripts also tentative suggest the presence of stress sensitivity – a heightened stress reactivity towards future stressors – following exposure to early life trauma (Harkness et al., 2015). Particularly regarding stress sensitivity, findings of Manuscript 3 and pertinent prior research studies might help to understand the mechanism of action underlying stress sensitivity. In Manuscript 3, individuals with prior exposure to potentially traumatic events showed a trend for increased FC within the SN. In terms of stress sensitivity this might suggest that following the exposure to potentially traumatic events, the rs-FC within the SN might become hyperreactivite in response to exposure to future stressors. In fact, previously the exposure to high levels of stress and increases stress sensitivity (e.g., high cortisol responses) were associated with an increase in the brain's stress response by means of increased medial temporal and amygdala response in an experimental stress paradigm (Henckens et al., 2016). Furthermore, it has been observed that individuals who displayed both a strong task-evoked amygdala response and task-free strong connectivity with the SN, reported the highest levels of arousal (Touroutoglou et al., 2014).

The hypothesis of stress sensitivity can be further brought in context with the observed low levels (trend level) of within-DMN rs-FC in individuals with probable PTSD in Manuscript 3. In more detail, a study on childhood poverty and stress reactivity revealed that the exposure

to early life adversity in the form of childhood poverty was associated with reduced DMN connectivity and a high cortisol response when facing future stressors (Sripada et al., 2014). In fact, it is assumed that the exposure to adversity during childhood increases the child's risk for developmental deficits in brain regions implemented in emotion and threat processing and thereupon when exposed to chronic stress alters the brain's response in the direction of heightened stress sensitivity for future stressors (McEwen & Gianaros, 2011). This is further in line with previous findings on altered DMN FC in association with low socio-economic status (Spreng et al., 2009) and differential FC of the SN following the exposure to childhood maltreatment (van der Werff et al., 2013). Hence, results of Manuscript 3 help to emphasize the importance of stress sensitivity in individuals following the exposure to potentially traumatic events on a neurobiological level.

Concluding on the results of the three manuscript, a clear strength was the implementation of several different forms of assessments in the present thesis: various self-reported measures (subjective physical health, exposure to child maltreatment, life stressors), a behavioral estimate (physical mobility), two cognitive estimates (general cognitive performance and language comprehension/verbal intelligence), a structured clinical interview (lifetime PTSD) and neurobiological underpinnings (ICNs) of networks previously shown to be involved following the exposure to potentially traumatic events and in association with PTSD symptoms. Altogether, results stemming from these various assessments revealed that the exposure to potentially traumatic events is associated with several post-traumatic stress responses such as the development of lifetime PTSD symptoms, lower cognitive functioning following the exposure to child maltreatment in the context of welfare care, lower physical functioning particularly following the exposure to child emotional neglect, and physical and sexual abuse, and rs-FC alterations (trend level) in the SN as well as the DMN in association with probable PTSD symptoms.

4.2 Limitations of the Present Thesis

In the following, limitations of the present thesis which have not yet been noted within one of the manuscripts will be addressed. Given the fact that samples were recruited locally (Swiss welfare care practices and Swiss healthy elderly individuals), caution should be applied when generalizing results. This is particularly true for the results of Manuscript 1 and Manuscript 2, as the nature of child welfare care practices, the contracting authority, and the societal context are known to have differed across countries. For instance, in Ireland and Austria the nature of child welfare care was greatly denounced by the Catholic Church, leading to themes of greater good and faith, which might have impacted the disclosure of child maltreatment incidences and thereupon on minors who reported against the Church (Carr et al., 2019, Lueger-Schuster et al., 2018) whereas in Switzerland societal threats such as weak yields and an increased fear of impoverishment need to be considered (Leuenberger & Seglias, 2013). Future studies could aim for a cross-national comparison to reveal common themes and differences between factors during and following exposure to institutional abuse.

Furthermore, given the evidence for PTSD symptom divergence and more subclinical symptom expression in older individuals, one could consider the fact that the assessment of lifetime PTSD, and not current PTSD symptomatology, in Manuscript 1 as a short coming. However, here it was decided to specifically assess lifetime PTSD to follow a life span approach in survivors of Swiss welfare care. Future research conducted with this sample might specifically focus on including individuals with present PTSD symptoms and thereupon investigate symptom divergence in survivors of Swiss child welfare care. Nevertheless, in Manuscript 3, a subclinical (healthy) older adult sample stemming from the Swiss general population was examined and the fact that PTSD might express differently in older individuals was tentatively acknowledged. Altogether the sample composition underlying this thesis might even be seen as a strength as two different study populations were examined. In the sample

underlying Manuscript 1 and Manuscript 2 half of the participants have been exposed to child welfare care practices which incorporated a high risk of exposure to severe forms of child maltreatment, whereas the second sample was comprised of non-clinical older adults revealing different levels of exposure to potentially traumatic events than was observed within the first sample.

4.3 Future Directions

The following three sections will outline recommendations for future research as well as clinical considerations and implications for policy and practice based on present findings, conclusions drawn from the literature, and ideas that evolved during the realization of the two research projects.

4.3.1 Future Directions: Research

The finding of perceived low levels of social acknowledgement in individuals with a history of institutional upbringing is consistent with the on-hand observations and participants' feedback during the conduction of the study. During the process of writing this thesis, the NRP76 follow-up measurement took place, which was further challenged by the global COVID-19 pandemic. As the mean age of the present NRP76 sample was above 70 years most participants were part of a high-risk group for the course and treatment of COVID-19. Nevertheless, it was overwhelming and surprising to witness the willingness to participate in the follow-up assessments during a global pandemic, particularly in the group of individuals with a history of institutional upbringing. Participants' testimonies revealed a strong aspiration to be heard and disclose their experiences. Given the fact that this chapter of Swiss history has just recently undergone societal reappraisal, there is much to suggest that affected individuals might benefit from ongoing work in this new era. Hence an avenue for future research with

survivors of institutional upbringing could be to conduct an intervention study aiming to tackle the reported low levels of social acknowledgement and thereupon improve the post-traumatic stress responses.

Furthermore, given the retrospective nature of the present data combined with the inability to draw causal links between maltreatment and health outcomes for abuse survivors, prospective longitudinal studies on the effects and outcomes of child maltreatment are warranted. Moreover, a growing body of research suggests that PTSD could also impact cognitive and physical health (Burri et al., 2013; El-Gabalawy et al., 2018; Ryder et al., 2018). Together with the present finding that the manifestation of lifetime PTSD symptoms is related to child maltreatment in a dose-response relationship, future research might benefit from examining lifetime PTSD symptomatology as a potential mediator between the exposure to child maltreatment and cognitive and physical functioning in older age.

In relation to neurobiological underpinnings, Manuscript 3 revealed that changes in the brain's functional organization can be observed in non-clinical older adult populations. As this was the first study to be conducted, the primary aim was to contribute to a more fundamental understanding in this regard. However, with increased understanding of age-related functional dedifferentiation (Zonneveld et al., 2019) and functional connectivity changes in association with potential trauma exposure and probable PTSD (Sheynin et al., 2020) future research studies could build upon present findings to conduct network subregion analysis in non-clinical samples to improve the specificity and resolution of the current data.

Furthermore, previous research findings suggest that rs-FC alterations depend on the type of exposure to potentially traumatic events. In more detail, exposure to early-life adversity has been shown to relate to lower between-network connectivity (Bluhm et al., 2009), whereas exposure to potentially traumatic events in later life (e.g., military exposure) was associated with greater between-network connectivity (Sripada et al., 2012). Hence an avenue for future

research could be to examine differences in rs-fMRI associated with the type of exposure to potentially traumatic events until older age.

Moreover, an interesting path for future research could be to combine the assumption underlying Manuscript 3, that aging involves a decrease in functional segregation (Malagurski et al., 2020), with the observation of lower physical functioning in older age following exposure to child maltreatment in Manuscript 2. This is interesting given previous findings on increased FC in age-sensitive resting-state brain regions following the performance of high levels of physical activity (Boraxbekk et al., 2016; Salami et al., 2014). Hence there is much to suggest that future research could reveal interesting findings when examining the potential beneficial effect of physical activity on the brain's FC in the context of aging following the exposure to potentially traumatic events.

4.3.2 Future Directions: Clinical Considerations

Several future clinical considerations can be drawn from the present thesis. First, given the near ubiquity of exposure to child maltreatment, clinicians should be better trained to detect and treat individuals following the exposure to child maltreatment in order to counteract the early momentum of cumulative adversity. In the same vein, and in line with the observation that individuals with a history of child maltreatment were also more prone to experience future stress exposure, special therapy options should be provided to individuals following initial exposure to adverse events particularly in the early phases of the life course, childhood and/or adolescence. Another clinical recommendation relates to providing reliable and valid questionnaires to assess social acknowledgement at the start of therapy to monitor perceived levels of social acknowledgement and thereupon to tackle low levels of social acknowledgment in therapy given the observation of the potential buffering effect of high levels of social acknowledgment on PTSD symptom manifestation.

Furthermore, during the process of conducting the semi-structured clinical interviews with the participants of the NRP76 study it became evident that many participants with a history of welfare care indicated their most detrimental potentially traumatic event to be the experience of emotional abuse and emotional neglect during their time in welfare care. As, however, the administered semi-structured clinical interview (DIPS) is based on DSM-IV criteria and the criteria A for PTSD does not cover emotional abuse and emotional neglect, the presence of probable PTSD symptoms within the last four weeks were not able to be assessed in the context of emotional abuse and neglect. This is in contrast to previous findings that describe the exposure to emotional abuse and neglect on its own can lead to aberrant post-traumatic stress responses. For instance, a research study examining type of trauma exposure and symptom severity (Glück et al., 2016) demonstrated that high rates of PTSD symptom severity were observed in individuals experiencing institutional abuse, including emotional abuse. Hence, it might be worth adapting the criteria A of the DSM as to also include the experiences of emotional abuse and neglect to fit the diagnostic threshold, and thereupon to offer prominent trauma therapy treatments to those who experience distressful symptoms following emotional abuse and neglect.

4.3.3 Future Directions: Implications for Policy and Practice

Furthermore, the rapidly aging population coupled with the potentially escalating costs of health and social care leads to an urgent need to reduce illness and disability in later life. A recommendation based on present findings relates to the enhancement of insurance policies in a way to specifically provide affordable and maybe even free-of-charge assistance to those stemming from less advantaged backgrounds. This is based on present findings and prior observation in which the accumulation of exposure to adversity and economic disadvantage influence mental, cognitive, and physical health, and specifically, functional capacities in older age. In a similar vein public interventions aimed to improve the accessibility of mental health

assistance in the form of psychotherapy and counseling would be desirable. As an example, following the reappraisal movement of Swiss welfare care practices, affected individuals were able to apply for monetary compensation (i.e., solidary contribution of CHF), however in this context it may be also helpful to offer affected individuals the option to visit advisory offices and counseling sessions when confronted with potential upcoming memories and stress responses.

Furthermore, there is a great need to ameliorate evidence-based child protection policies and practices to prevent the exposure to child maltreatment and related consequences for health. For frontline professionals such as childcare staff and foster parents, a more careful selection, increased training programs, and a higher level of supervision should be implemented to improve child protection practices.

4.4 General Conclusion

This thesis provides a novel contribution to the literature of health associates that persist into older age following the exposure to child maltreatment and/or the exposure to potentially traumatic events. The first paper contributes to current understanding of lifetime PTSD symptomatology following different levels of exposure to child maltreatment also within the context of institutional upbringing and highlights the importance of socio-interpersonal factors namely social acknowledgement following the exposure to potentially traumatic events. The second paper expanded on this work by further examining cognitive and physical functioning following the exposure to child maltreatment until older adulthood. Overall, findings from Manuscript 1 and Manuscript 2 suggest that individuals affected by Swiss welfare care practices in their childhood and/or adolescence might have been prone to be affected by a triad of risk factors. The first risk factor relates to the fact that the placement of minors into welfare care settings was associated with a high risk to having been exposed to severe forms of child

maltreatment. The second risk factor relates to the observation that high levels of exposure to child maltreatment were associated with higher levels of lifetime PTSD symptoms and the mere reporting of life stressors in adulthood. Third, when having experienced severe forms of child maltreatment, and having undergone several life stressors, individuals were more likely to experience lower levels of physical functioning in older age. Manuscript 3 expanded on this work and investigated for the first-time neurobiological underpinnings by means of intrinsic FC following the exposure to potentially traumatic events and in association with PTSD symptoms in a non-clinical older adult population. Results of this third manuscript revealed that also in non-clinical older adult populations, alterations in within-DMN and within-SN rs-FC can be observed following the exposure to potentially traumatic events and in association with probable PTSD symptoms.

Overall, the present findings further our understanding on the exposure to potentially traumatic events and its associations with various post-traumatic stress responses such as the development of lifetime PTSD symptoms, lower cognitive functioning following the exposure to child maltreatment in the context of welfare care, lower physical functioning particularly following the exposure to child emotional neglect, physical and sexual abuse and rs-FC alterations in the SN as well as the DMN in association with probable PTSD symptoms. I hope that the present findings stimulate a fruitful discussion on how to probe neurobiological signatures following the exposure to potentially traumatic events and in association with probable PTSD and form the basis for future research efforts on how to study amendments in perceived levels of social acknowledgement following the exposure to potentially traumatic events.

5 PUBLICATIONS

5.1 Manuscript 1: Lifetime Post-Traumatic Stress Disorder in Older Individuals With a History of Institutional Upbringing in Childhood: The Role of Social Acknowledgement and Stressful Life Events

Carla M. Eising[1,2*], Manuel C. Voelkle[3], Shauna L. Rohner[1,2], Andreas Maercker[1,2], & Myriam V. Thoma[1,2]

[1]University of Zürich, Psychopathology and Clinical Intervention, Institute of Psychology, Binzmühlestr. 14 / 17, 8050 Zürich, Switzerland

[2]University Research Priority Program "Dynamics of Healthy Aging", University of Zürich, Zürich, Switzerland

[3]Humboldt University of Berlin, Rudower Chaussee 18, 12489 Berlin, Germany

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Abstract

Background: Child maltreatment (CM), particularly in institutional contexts, can affect the development of post-traumatic stress disorder (PTSD). Research suggests that factors during CM (e.g., severity, variety, duration) and in the aftermath of CM (e.g., stressful life events, and social acknowledgment, i.e., the degree to which an individual feels validated and supported following a traumatic event) can explain some of the heterogeneity in PTSD development. However, there is a lack of research on long-term correlates of CM and mitigating factors, with only a few studies having been conducted with older survivors of institutional upbringing. Such research is relevant, given the long-term associations between CM and the older age status of many survivors.

Objective: The current study examined the link between CM and PTSD in older individuals with a history of institutional upbringing (risk group; RG) and a matched control group (CG). Differences in stressful life events and social acknowledgment were also investigated.

Method: Participants were n=116 RG (M_{age}=70.25 years, 41% female) and n=122 CG (M_{age}=70.71 years, 51% female). Data was assessed using self-report questionnaires and a clinical interview.

Results: The RG reported higher levels of exposure to CM. Lifetime PTSD showed a bigger association with the level of exposure to CM, compared to having an institutional upbringing. Participants with higher CM levels reported more stressful life events. High levels of social acknowledgement mediated the relationship between CM and PTSD in the CG.

Conclusions: Exposure to CM had a stronger association with PTSD than a history of institutional upbringing. In the CG, the survivors' perception of social acknowledgment ameliorated lifetime PTSD to a small extent. A critical issue for policy makers should be to enhance safeguarding measures against CM exposure, not only in institutional contexts, but also more generally, given the link to PTSD.

Keywords**:** Child maltreatment, institutional upbringing, post-traumatic stress disorder, social acknowledgement, stressful life events, older individuals.

Lifetime post-traumatic stress disorder in older individuals with a history of institutional upbringing in childhood: The role of social acknowledgement and stressful life events

1. Introduction

Mounting evidence suggests that maltreatment in childhood and/or adolescence can lead to long-term negative mental health correlates (Norman et al., 2012). A specific long-term detrimental impact of child maltreatment (CM) is the development of post-traumatic stress disorder (PTSD; Krammer, Kleim, Simmen-Janevska, & Maercker, 2016). For instance, the review by Messman-Moore and Bhuptani (2017) on CM history and PTSD prevalence showed that individuals who were exposed to childhood sexual and emotional abuse displayed a higher PTSD prevalence in adulthood compared to other types of CM. Furthermore, a systematic review on the outcomes of CM in long-term care showed that CM is linked to PTSD and other adverse outcomes (e.g., anxiety disorder), not only in adulthood, but into older age (Carr, Duff, & Craddock, 2020a). However, not all individuals affected by CM develop PTSD or other maladaptive mental health outcomes over the life course. For instance, in a large, case-control study on adults with and without CM, 22% of those who reported CM showed a resilient trajectory without any ill-health conditions (McGloin & Widom, 2001). To understand this heterogeneity in the development of PTSD, previous research has closely examined various aspects of the CM experience, including factors during CM (e.g., severity, variety, context) and subsequent to CM exposure (e.g., life stressors).

Often discussed in the context of CM and PTSD, is the proposed 'dose-response' relationship, investigated through factors of CM including the severity, variety, and duration (Norman et al., 2012). For instance, a study on CM and mental disorders showed that more severe CM was associated with higher subsequent PTSD prevalence (Duran et al., 2004). Similarly, research has shown a cumulative effect of CM on PTSD development, as the

prevalence rate of PTSD appears to increase with the number of experienced CM types (Clemmons, Walsh, DiLillo, & Messman-Moore, 2007); as well as the duration of CM exposure (Kaysen, Rosen, Bowman, & Resick, 2010). However, several studies are challenging this assumption of a simple dose-response relationship. For example, recent findings in the polyvictimization literature highlight the importance of contextual aspects of the CM exposure, such as the setting or the context within which CM has occurred (e.g., unique types of victimization; Adams & Allwood, 2020; Ayer et al., 2019). These contextual factors also need be considered in order to understand the heterogeneity in the development of PTSD after CM.

Existing research within the field of CM, suggests that the long-term correlates of CM can differ depending on the context within which CM was experienced. For instance, a recent study that examined the long-term correlates of CM with institutional survivors and a control group showed that institutional survivors were significantly more likely to be affected by lifetime and current PTSD than control participants (Lueger-Schuster et al., 2018). Furthermore, two studies examining the past-year PTSD prevalence in adults with an institutional upbringing showed that PTSD prevalence ranged from 11.7% to 25% (Courtney, Dworsky, Cusick, Havlicek, Perez, & Keller, 2007; Pecora, et al., 2005). These figures are considerably higher than the PTSD prevalence of 1.1% to 2.9% in the general population (Trautmann & Wittchen, 2018). In explaining such disparities in PTSD, some research has emphasized the high levels of exposure to CM in these care settings (Carr, et al., 2020b; Hermenau, Eggert, Landolt, & Hecker, 2015). However, it remains unclear whether it is the higher level of exposure to CM within these institutions that contribute to the high lifetime PTSD rates; or if the contextual aspects of CM exposure in such institutions also play a role, such as the lack of a stable caregiver (Carr, Duff, & Craddock, 2020b), institutional hierarchy (Smith & Freyd, 2014), or stigmatization (Lueger-Schuster et al., 2018). In addition to these factors during CM exposure, potential compounding factors in later-life, such as adult trauma

and life stressors, also need to be considered when investigating the long-term correlates of CM (Burri, Maercker, Krammer, & Simmen-Janevska, 2013).

Research has repeatedly shown that initial disadvantage, such as CM, can increase the likelihood for future stress exposure (Scott-Storey, 2011). In particular, the proposed higher exposure to CM in institutions may be associated with more later-life stressors in affected individuals. This is in line with previous research in which survivors of institutional CM reported higher exposure to adult stressful life events than control participants (Lueger-Schuster et al., 2018). However, little is known about whether the observed higher rates of adult stressful life events in institutional survivors are linked to the increased exposure to CM within institutions or the placement of individuals into the institutional environment (e.g., malnutrition, poor education; Carr, et al., 2020b).

One important aspect that has been found to be associated with the development of PTSD following CM exposure is social acknowledgement. Social acknowledgement is a construct that describes the degree to which an individual feels validated and supported by society, family, and friends following a traumatic event (Maercker & Hecker, 2016). In comparison to social support, social acknowledgement does not encompass the functional (e.g., emotional validation) or structural aspects (e.g., size or composition of social network) of the individual's life circumstances; but rather focuses on the individual's perception of their recognition as a survivor (e.g., general or familial recognition or disapproval; Mueller, Moergeli, & Maercker, 2008). This is in line with a recent study examining a social model of PTSD, where social acknowledgement was found to be related to posttraumatic cognitions, as compared to other related processes of social support such as emotional disclosure and group identification (Woodhouse, Brown, & Ayers, 2018). Previous studies have identified social acknowledgment as both a predictor of PTSD symptomatology, as well as a factor that reduces post-traumatic stress. For example, in a study on recovery from post-traumatic stress, social

acknowledgement was found to be a strong predictor of PTSD symptoms post-crime (Mueller et al., 2008). In addition, a study on a web-based intervention for social acknowledgement showed that social acknowledgement led to a reduction in PTSD symptomatology following a one-month intervention (Xu et al., 2016). Furthermore, in a recent study on patient assaults on Chinese emergency nurses, social acknowledgment was found to mediate the relationship between frequency of patient assaults and PTSD symptoms (Guan, Gao, Liu, Cheng, & Ge, 2019). To the best of the authors knowledge, only one study has previously examined social acknowledgment as a mediator of post-traumatic stress in an institutional sample (Krammer et al., 2016). In this study on childhood traumatic events and PTSD witholder individuals, social acknowledgement partially mediated the relationship between childhood traumatic events and PTSD. However, this study lacked a control group, which hinders specific conclusions on the level of exposure to CM, its relationship with social acknowledgement, and potential differences between institutional survivors and controls. Furthermore, the institutional group was a very specific sample of individuals affected by indentured child labor, and other forms of institutionalized child welfare contexts were not investigated. This limited the generalization of the results to other individuals affected by institutional child welfare contexts.

1.5 Aims of the Study

To address these gaps in the literature on CM and PTSD, this study investigates the link between CM and lifetime PTSD in individuals from institutional child welfare contexts. Specifically, it is hypothesized that individuals with a history of institutional upbringing will show higher levels of exposure to CM and lifetime PTSD, compared to individuals with no history of institutional upbringing. Furthermore, it is hypothesized that higher levels of CM exposure will be linked to a higher number of adult stressful life events, and that this association will be pronounced in the institutional group compared to the control group, due to the

proposed higher level of CM exposure in institutional settings. Finally, the study aims to examine the potential dampening or exaggerating effect of social acknowledgement on the relationship between CM and lifetime PTSD. It is hypothesized that individuals with a history of institutional upbringing will report lower levels of social acknowledgement, compared to individuals in the control group. In addition, it is hypothesized that in the institutional group, the expected low levels of social acknowledgement will be linked to an exaggerating effect on the relationship between CM and lifetime PTSD; whereas in the control group, it is expected that high levels of social acknowledgment will be linked to a dampening effect on the relationship between CM and lifetime PTSD.

2. Methods

The current study was conducted within the larger project "Differential aging trajectories in high-risk individuals with past experiences of early adversity", which is part of the National Research Program "Welfare and Coercion – Past, Present and Future" (NRP76). The study protocol was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the University Zürich (ID:19.4.3).

2.1 Participants

A total of $N = 250$ individuals were recruited for the present study. All participants provided informed consent. Half were affected by compulsory social measures and placements (CSMP) in childhood and/or adolescence, referred to as the risk group (RG). The other half were an age-matched control group (CG). Inclusion criteria were Swiss-German speaking and a minimum age of 50 years. Fifty years was chosen as the minimum age to capture the potential start of age-related decline (e.g., physical, cognitive functioning) and in an attempt to minimize any potential survivor bias (Mc Gee, Höltge, Maercker, & Thoma, 2018). In the RG,

participants had to have been affected by CSMP for at least one year, before 18 years of age. In Switzerland, CSMP were ordered by the administrative authorities to counteract the growing economic threat due to weak crop yields, lengthy famines, and the increasing impoverishment of the population (Federal Office of Justice, 2020). Generally for adolescents, CSMP involved forced placements into closed penal facilities, detention centers, psychiatric institutions, as well as enforced adoptions and compulsory medical procedures (e.g., mandatory sterilization, forced abortion, or compulsory drugging; Federal Office of Justice, 2020). Children were often placed into foster families or children's homes, where it was common practice that minors had to work for their daily living (e.g., farming, dairy; Leuenberger & Seglias, 2008). For a detailed description of CSMP practices in Switzerland, see the recent study on the long-term mental and physical health correlates of these older survivors of child welfare practices (Thoma, Bernays, Eising, Pfluger, & Rohner, 2020).

2.2 Recruitment

During the application process for the solidary contribution, individuals affected by CSMP could indicate whether they wanted to be contacted in future for research purposes on the broader topic of CSMP. The last author of this paper (MVT) received a list of these individuals from the Federal Office of Justice. Then in timed intervals between July and November 2019, letters were sent to $N = 495$ individuals. These letters contained the description and aim of the study, as well as the contact information of the study team. From these individuals, $n = 116$ were interested in participating in the study. Additional recruitment took place through the oral snowballing principle and the posting of the project flyer on websites and distributed per online mail.

Participants in the CG were recruited via posted flyers and advertisements on websites directed at older adults, as well as through contacts of the study team. In addition, participants

in the CG were also recruited from the participant pool of the affiliated University Research Priority Program (URPP) 'Dynamics of Healthy Aging' at the University of Zurich.

2.3 Procedure

Interested individuals called the study phone and were informed about the study aim and procedures. Individuals were then screened for the inclusion criteria and two face-to-face appointments were scheduled. Depending on the participant's preference, the appointments were conducted at Zürich University or the participants' home. At the first assessment (A1), all participants provided informed consent and then completed the Diagnostic Interview for Mental Disorders (DIPS), as well as an additional assessment of CSMP-related information for the RG. All interviewers were trained in conducting the DIPS and were supervised by the last author, who is a psychotherapist with years of clinical experience. At the second assessment (A2) participants completed questionnaires on life adversity, coping, as well as behavioral and cognitive assessments. Upon completion of A2, participants received a compensation of approximately $250.

2.4 Measures

2.4.1 Socio-Demographic Information – Socio-demographic information included age, gender, education, and specific questions for the RG regarding their CSMP background (e.g., initial age, duration).

2.4.2 PTSD – PTSD was assessed using the open access Diagnostic Interview for Mental Disorders (DIPS; Margraf, Cwik, Pflug, & Schneider, 2017; Margraf, Cwik, Suppiger, & Schneider, 2017). The PTSD section of the DIPS begins by asking about exposure to 19 potentially traumatic events across the life span (e.g., physical abuse in childhood, sexual abuse in adulthood, life-threatening disease). A PTSD diagnosis was given when all DSM-5 criteria

(A-H) were fulfilled (APA, 2013). Subthreshold PTSD was given in accordance with the proposed *Definition-1* by Franklin, Raines, Chambliss, Walton, and Maieritsch (2018), which required criteria A, B, C, and either D or E to be fulfilled. The DIPS has shown moderate agreement between patients and relatives on PTSD diagnosis over the life course ($\kappa = 0.57$; Cwik et al., 2018).

2.4.3 Child Maltreatment and Stressful Life Events – The German version of the *Traumatic Experience Checklist* (TEC) assessed traumatic and stressful life experiences in childhood, adolescence, and adulthood (Nuijenhuis, Van der Hart, & Kruger, 2002). Following the manual by Nijenhuis (2017), separate scores were calculated for each CM type (e.g., emotional neglect, emotional abuse, physical abuse), as well as a 'total CM exposure' score encompassing all CM types and incorporating various aspects of trauma exposure (e.g., severity, variety, duration). Furthermore, a sum score of stressful life events over the life course was also calculated with the TEC based on the presence of 20 stressful life events. Higher values indicate more stressful life events.

2.4.4 Social Acknowledgement – Social acknowledgement was measured using the German 16-item *Social Acknowledgement Questionnaire* (SAQ; Maercker & Mueller, 2004). The SAQ captures an individual's perception of their recognition as a victim or survivor following a traumatic event, as well as perceived support from family, friends, and society. Responses are recorded on a 4-point Likert scale ranging from 0 (not at all) to 3 (completely). In the current study, the SAQ showed high internal consistency across the subscales, with the following Cronbach's alphas: general disapproval ($\alpha = .74$), recognition ($\alpha = .74$), family disapproval ($\alpha = .70$).

2.5 Data Analysis

Analyses were performed using the Statistical Package for Social Sciences (SPSS) version 25.0 (IBM Corp., 2017) and the PROCESS macro for SPSS version 3.0 (Hayes, 2018). Only individuals with a lifetime history of trauma (n = 195) answered the SAQ. For those who did not report a lifetime history of trauma (n = 43; RG n = 22, CG n = 21), the SAQ values were imputed with the value zero, reflecting the lack of a specific impact from a traumatic experience following Schafer and Graham (2002). On all measures, there were less than 5% missing values due to item nonresponse, with Little's missing completely at random (MCAR) test indicating the nonresponses to be MCAR. Accordingly, missing values were replaced using the Expectation-Maximization algorithm (Dempster, Laird, & Rubin, 1977). Group differences in gender and education were calculated using χ^2-test statistics. To examine the link between CM and lifetime PTSD, Spearman's rho correlations were performed, and separate linear regression analyses were conducted for the RG and the CG. To examine the quantity of stressful life events, separate linear regression analyses were conducted for the RG and CG. To examine differences in the level of social acknowledgement between the RG and CG, a linear regression analysis was conducted. To assess social acknowledgment as a mediator between CM and lifetime PTSD for the RG and CG, separate mediation analyses were performed (model 4 using one mediator), with confidence intervals calculated using bootstrapping (number of bootstrap samples = 5000). To determine the minimum required effect size to ensure adequate power in line with recommendations (e.g., Cohen, 1992), a sensitivity power analysis was conducted for the present study. With an alpha level of 5% and a power of 80%, the minimum effect size was f = 0.18 for a sample size of N = 238. According to common conventions (e.g., Cohen, 1992), this corresponds to a small to medium effect size, which is of high practical importance in the field (Weber, Jud, & Landolt, 2016).

3. Results

3.1 Sample Characteristics

The final sample consisted of N = 238 older adults, as data on CM was missing for 12 participants, who were excluded from the analysis. The RG (n = 116) had a mean age of 70.25 years (SD = 12.47) and the CG (n = 122) had a mean age of 70.71 years (SD = 9.63). Socio-demographic data are displayed in Table 2.

Table 2

Socio-Demographic Characteristics

Sample Characteristics	Total Sample (N = 238)		Risk Group (n = 116)		Control Group (n = 122)		χ^2	*df*	*p*
	N	%	*N*	%	*N*	%			
Sex							2.51	1	.073
Male	127	53.4	68	58.6	59	48.4			
Female	111	46.6	48	41.4	63	51.6			
Education							47.81	7	.000***
No education	5	2.1	5	4.3	0	0			
Primary school	9	3.8	8	6.9	1	0.8			
Upper secondary school	24	10.1	19	16.4	5	4.1			
High school	6	2.5	2	1.7	4	3.3			
Vocational job training	93	39.1	50	43.1	43	35.2			
Higher professional training	37	15.5	18	15.5	19	15.6			
University	52	21.8	7	6.0	45	36.9			
Other	12	5	7	6.0	5	4.1			
	M	*SD*	M	*SD*	M	*SD*	F	*df*	*p*
Age	70.5	11.1	70.2	12.4	70.7	9.6	18.8	236	.75

Note. χ^2 = Chi-squared test, *df* = degrees of freedom, *p* = p value, *M* = mean, *SD* = standard deviation, *F* = test for variance, *** $p < .001$.

3.2 Child Maltreatment, Group, and Lifetime PTSD

In the following section, the association between CM and lifetime PTSD symptomatology across both groups is first investigated. In a next step, group differences in CM and lifetime PTSD symptomatology are assessed. Lastly, it is examined whether the level of exposure to CM and/or group membership are associated with lifetime PTSD symptomatology.

Table 3

Means and Intercorrelations of Child Maltreatment and Lifetime Post-Traumatic Stress Disorder Across Groups

Variable	*M*	*SD*	1	2	3	4	5	6
1. Emotional neglect	6.39	5.25	-	.616***	.497***	.194***	.244***	.265***
2. Emotional abuse	5.29	5.23		-	.708***	.258***	.291***	.333***
3. Physical abuse	4.57	4.73			-	.271**	.323***	.307***
4. Sexual abuse	0.97	2.19				-	.477***	.247***
5. Sexual harassment	1.33	2.16					-	.160**
6. Lifetime PTSD		-	.265***	.333***	.307***	.247***	.160**	-

Note. M = mean, SD = standard deviation, PTSD = post-traumatic stress disorder, ** $p < .05$, *** $p < .001$.

Across both groups, participants with a higher total CM exposure and higher scores on each CM type showed significantly higher lifetime PTSD symptomatology compared to those with lower total CM exposure (see Table 3 for means and intercorrelations). Furthermore, regression analyses revealed that the RG reported higher levels of exposure to CM compared to the CG, ($R^2 = .124$, F (1,237) = 33.54, $p < .001$) (see Table 4 for means and standard deviations).

Table 4

Means and Standard Deviations of Child Maltreatment Type per Group

Child Maltreatment Type	Risk Group		Control Group		R^2
	M	*SD*	*M*	*SD*	
Emotional neglect	8.09	4.61	4.76	5.30	.102***
Emotional abuse	6.61	4.89	4.03	5.26	.061***
Physical abuse	5.91	4.24	3.29	4.83	.077***
Sexual abuse	1.30	2.29	0.66	2.05	.022**
Sexual harassment	1.97	2.46	0.71	1.62	.083***

Note. M = mean, *SD* = standard deviation, R^2 = adjusted variance explained, risk group n = 116, control group n = 122, ** $p < .05$, *** $p < .001$.

Regression analysis revealed a significant effect of group on lifetime PTSD ($R^2 = .039$, F (1,237) = 9.60, $p < .05$). This indicates that the RG showed higher lifetime PTSD scores compared to the CG (see Table 5 for prevalence rates of PTSD per group). When controlling for total CM exposure in the analysis of variance in lifetime PTSD by group, the incremental effect of group within the model was not significant ($p > .05$), indicating that group does not independently contribute to the explanation of variance in lifetime PTSD.

Table 5

Prevalence Rates of Lifetime Post-Traumatic Stress Disorder Across Both Groups, and Separately for the Risk and Control Groups

Sample	PTSD Diagnosis					
	None		Subthreshold		Full	
	N	%	*N*	%	*N*	%
Total (*N* = 238)	178	74.8	13	5.5	47	19.7
Risk Group (*n* = 116)	76	65.5	9	7.8	31	26.7
Control Group (*n* = 122)	102	83.6	4	3.3	16	13.1

Note. *N* = number and % = percentage of participants who fulfilled the diagnosis category, PTSD = post-traumatic stress disorder, Subthreshold = in accordance with the definition by Franklin et al. (2018), Full = when all DSM-5 criteria (A-H) were fulfilled.

3.3 Stressful Life Events

With regard to stressful life events, this study examined whether there were differences in the level of adult stressful life events depending on the level of exposure to CM, and between individuals from institutional contexts and controls.

Across both groups, participants with higher levels of total CM exposure reported significantly more stressful life events than those with lower total CM exposure (R^2 = .057, F (1,226) = 13.66, p <. 001). No significant differences in stressful life events were observed between the RG and CG (R^2 = .014, F (1,237) = 3.09, p >. 05) (see Table 6 for bivariate correlations).

Table 6

Bivariate Correlations Between Child Maltreatment and Stressful Life Events, separately for the Risk and the Control Group

Variable	1	2	3	4	5	6
Risk Group						
1. Emotional neglect	-	.587***	.499**	.107	.203**	.203**
2. Emotional abuse		-	.628***	.214**	.296***	.363***
3. Physical abuse			-	.176	.304***	.336***
4. Sexual abuse				-	.675***	.247**
5. Sexual harassment					-	.269***
6. Stressful life events						-
Control Group						
1. Emotional neglect	-	.584***	.411***	.204**	.138	.032
2. Emotional abuse		-	.733***	.251***	.174	.018
3. Physical abuse			-	307***	.236**	.047
4. Sexual abuse				-	.124***	.044
5. Sexual harassment					-	.072
6. Stressful life events						-

Note. ** $p < .05$, *** $p < .001$.

3.4 Social Acknowledgement

With regard to social acknowledgement, this study examined whether, a) individuals in the RG showed lower levels of social acknowledgement compared to the CG; and b) whether these differences were associated with the prevalence rates of lifetime PTSD.

Regarding group differences, the regression analysis revealed a significant effect of group on social acknowledgment ($R^2 = .112$, $F\,(1,237) = 29.85$, $p < .001$), indicating that the RG reported less social acknowledgement compared to the CG. In a next step, total CM exposure was added

to the model to investigate the relative contribution of group and CM in explaining the incremental variance in social acknowledgement. This model explained a higher proportion of variance in social acknowledgement than group membership alone (R^2 = .155, F (2,237) = 21.57, p < .001) (see Table 7 for the analysis of social acknowledgement by CM and group).

Table 7

Regression Analysis of Social Acknowledgement by Child Maltreatment and Group

Predictors	Social Acknowledgment			
	B	*SE*	*t*	*p*
Constant	5.49	.68	8.06	< .001
Group	-3.43	.85	-4.12	< .001
Total Child Maltreatment Exposure	-.10	.03	-3.45	< .001
Observations	*N* = 237			
R^2	.155			
R^2 adjusted	.148			

Note. *N* = number of participants, R^2 = goodness-of-fit measure, R^2 adjusted = goodness-of-fit measure corrected, B= slope, SE= standard error, *t* = t-test, *p* = p value.

In the CG, a significant total effect was observed between total CM exposure and lifetime PTSD (*b* = .025, 95% CI [.0172, .0328], *t.*= 6.382, *p* < 0.01), explaining 25.34% of the variance in lifetime PTSD. When social acknowledgement was included as a mediator, a significant direct effect emerged, explaining a higher percentage of variance (29.41%). A significant indirect effect was also observed, indicating that social acknowledgement acts as a partial mediator in the relationship between total CM exposure and lifetime PTSD (*b* = .0037, 95% CI [.001, .008]). Similarly, in the CG, social acknowledgement significantly partially mediated the relationship between CM types and lifetime PTSD: emotional neglect (*b* = .0219, 95% CI

[.006, .041]), emotional abuse (*b* = .0163, 95% CI [.004, .032]), physical abuse (*b* = .0152, 95% CI [.003, .029]), and sexual abuse (*b* = .0297, 95% CI [.008, .082]). Sexual harassment was not significantly mediated by social acknowledgment in the CG ($p > .05$). See Figure 2 for the mediation models of the relationship between CM types, social acknowledgement, and lifetime PTSD. In the RG, social acknowledgment did not significantly mediate the relationship between any CM type or total CM exposure and lifetime PTSD ($p > .05$).

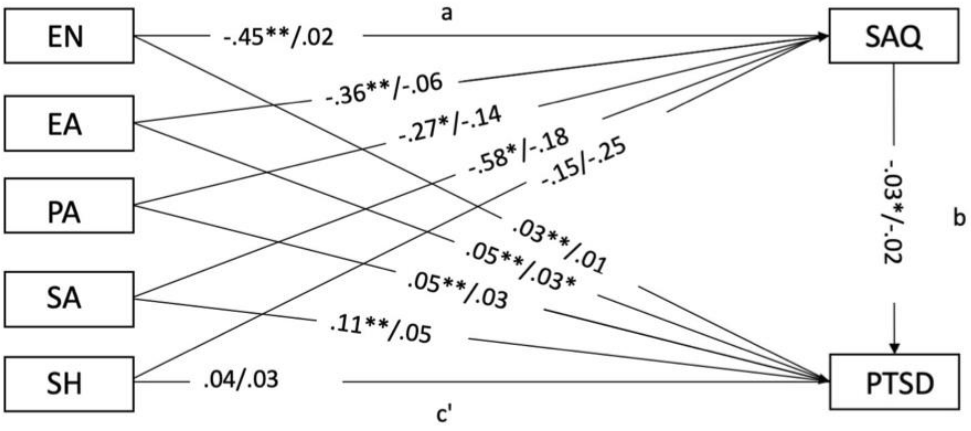

Figure 2. Mediation models of the relationships between abuse and neglect types (predictors) and lifetime post-traumatic stress disorder (outcome variable) across both groups, mediated by social acknowledgement.

4. Discussion

This study investigated the link between CM and lifetime PTSD in older individuals from institutional contexts and an age-matched control group. Results revealed that across both groups, individuals with higher levels of CM exposure reported higher lifetime PTSD. Furthermore, individuals from institutional contexts (i.e., RG) reported higher levels of CM exposure compared to control participants. Interestingly, the level of CM exposure showed a stronger association with lifetime PTSD than a history of institutional upbringing. Moreover, the relationship between CM and lifetime PTSD was mediated by social acknowledgment only in the control group, who also reported higher levels of social acknowledgment compared to

the institutional group. Across both groups, individuals with higher levels of CM exposure reported more stressful life events over the life course.

4.1 Child Maltreatment and Lifetime PTSD

The study finding of higher lifetime PTSD in individuals with higher levels of CM exposure is in line with previous research. More precisely, previous literature has repeatedly demonstrated a dose-response relationship between multiple factors during CM exposure and PTSD, including severity (Steine et al., 2017), variety (Bosch et al., 2020), and duration (Kaysen et al., 2010). However, in the present study, these CM-related factors (e.g., severity, variety, duration) were not examined separately as in the above-mentioned studies, but rather investigated in form of a composite CM score that takes into account multiple factors during trauma exposure (Nuijenhui et al., 2012).

4.2 The Importance of the Context of Child Maltreatment

The individuals from institutional contexts reported higher levels of CM exposure compared to controls. This finding is supported by previous research on the placement of minors within welfare care. For instance, in a study on institutional child abuse by the Roman Catholic Church, survivors reported abuse rates up to six times greater than individuals with no history of institutional care (Langeland, Hoogendoorn, Mager, Smit, & Draijer, 2015). Further support stems from the systematic review on CM in long-term care (Carr et al., 2020b), which showed that survivors of institutional upbringing reported severe forms of emotional neglect (e.g., emotional unresponsiveness), physical neglect (e.g., malnutrition), emotional abuse (e.g., constant rejection), physical abuse (e.g., punching), and sexual abuse (e.g., forced touching) during their time in institutional care. In accordance with this existing literature, the Swiss

institutionalized sample was also exposed to higher level of CM compared to a control group of the general population.

4.3 Institutional Contexts and Lifetime PTSD

The present study showed that the institutional group reported higher lifetime PTSD (26.7%) compared to the control group (13.1%). This is consistent with previous study findings of high lifetime PTSD (56.4%) in an Austrian foster care group compared to a control group (< 1%), which also assessed PTSD with a structured clinical interview for DSM-IV (Lueger-Schuster et al., 2018). With regard to the institutional samples, lifetime PTSD rates were higher in the Austrian sample than in the present study. However, in the Austrian sample, the foster care group was specifically recruited with the goal of finding survivors of institutional abuse; whereas these individuals in the present study had to be affected by institutional upbringing, but not necessarily by institutional abuse. These different recruitment strategies may have resulted in differences in exposure to institutional abuse and thus, also in PTSD. With regard to the control group, the lifetime PTSD rate was considerably high when compared to the control group in the study by Lueger-Schuster et al. (2018); and also, in comparison to the 12-month PTSD prevalence rates (1.1% - 2.9%) observed in the general European population (Wittchen et al., 2011). Future investigations that estimate PTSD prevalence may benefit from additionally incorporating the relatively new concept of complex PTSD (Karatzias et al., 2017). This may help capture more accurate prevalence rates of PTSD in the general population, which may be confounded by comorbid and unexamined conditions.

4.4 Institutional Contexts, Child Maltreatment, and Lifetime PTSD

In the current study, the level of CM exposure posed a higher risk for lifetime PTSD over and above having been brought up within institutional contexts. Here it is important to mention that

in addition to relatively high rates of PTSD in the control group, level of exposure to CM was also relatively high. More specifically, in the control group, 55.2% reported having been affected by emotional abuse, 57.6% by emotional neglect, 51.2% by physical abuse, and 20.8% by sexual abuse. In comparison, in the institutional group, 80% reported emotional abuse, 82.3% emotional neglect, 76.2% physical abuse, and 40.8% sexual abuse. When compared to the Austrian control group sample (Lueger-Schuster et al., 2018), this is a much higher level of exposure to CM in the present control group. Additionally, in the present study no differentiation was made between institutional and intra-familial CM in the institutional group. Hence, it may be that individuals in the institutional group experienced both institutional CM and intra-familial CM. As such, it is not possible to conclude with certainty that the high PTSD rates are associated with the level of CM exposure, and not due to additional contextual factors (i.e., intra-familial vs. institutional setting) during the exposure to CM. Future investigations may benefit from differentiating between and comparing institutional vs. intra-familial factors more closely, so as to increase the knowledge on the long-term correlates of institutional upbringing into older age. Furthermore, future investigations should acknowledge manual-specific PTSD differences, as previous research has shown that divergent diagnostic thresholds may be observed (Bruckmann, Haselgruber, Sölva, & Lueger-Schuster, 2020).

4.5 Stressful Life Events

Across both groups in the current study, individuals with higher levels of CM exposure reported higher rates of adult stressful life events. This is consistent with the stress sensitivity hypothesis of depression (Hammen, 2015), which states that individuals with a history of early adversity are more prone to develop a depressive episode during low levels of stress, compared to individuals without such a history. In the context of stress exposure, this can lead to a heightened stress awareness perception (i.e., subjective perception of more stressful life events over the life course; Hammen, 2015). In contrast to expectations, the groups in the current study

did not significantly differ with regard to number of stressful life events. Nevertheless, previous research on post-abuse events have shown that individuals with a history of institutional upbringing were more prone (than controls) to certain types of later-life stressors, such as physical assaults and serious injuries (Lueger-Schuster et al., 2018). This can also be seen in the present findings, as the institutional group reported more instances of serious physical injury than the control group. It may be that individuals with a history of institutional upbringing are particularly susceptible to certain types of stressors throughout their later life course (e.g., physical injury or illness). Future studies may benefit from investigating incidences of specific types of stressful life events to better inform preventative measures.

4.6 Social Acknowledgement

A novel observation in this study was that the institutional group reported a lower level of social acknowledgement than the control group. In light of the higher CM exposure in the institutional group, it may be that higher CM exposure is linked to lower social acknowledgment; suggesting that only with lower levels of CM exposure can survivors best perceive beneficial levels of social acknowledgement from their environment. However, more research is needed to support this speculative statement. Furthermore, social acknowledgment partially mediated the relationship between CM and lifetime PTSD in the control group. This is in line with findings from a previous study on social acknowledgement and disclosure, in which social acknowledgment was shown to mediate PTSD symptoms from pre-test to post-test (Xu et al., 2016). However, in the current study, this mediation effect was only observed in the control group. Future intervention studies may reveal important insights by investigating which levels of social acknowledgement are optimal for promoting post-trauma recovery in CM survivors. Contrary to our hypothesis, social acknowledgement did not exert an exaggerating mediating effect on the CM and PTSD relationship in the institutional group. This

was initially hypothesized as research has shown a reluctance towards social acknowledgment of institutional betrayal (Smith & Freyd, 2014); and in Switzerland the social acknowledgment of institutional CM is still a relatively recent phenomenon (Federal Office of Justice, 2020). However, it may be that in the context of CM, social acknowledgement exerts a buffering effect rather than an exaggerating effect on PTSD over the life course. More research is needed to examine the potential buffering and exaggerating effects of social acknowledgement in CM survivors.

4.7 Limitations and Strengths

There are several limitations in the current study that have to be critically considered when interpreting the findings. First, given the cross-sectional, retrospective study design, no causal inferences can be made. Additionally, the data on CM could have been affected by a memory recall and retrieval bias (Sheikh, 2018). However, a recent study on autobiographical memory recall examined traumatized individuals of advanced age (mean age = 72 years) with and without PTSD, as well as non-traumatized individuals. Results found no differences with respect to memory recall (Wittekind et al., 2017). Thus, while there may be the potential for memory biases in our older adult sample due to the retrospective design, it may be assumed that both groups are comparably affected due to the same mean age of both samples. Second, the sample recruitment might have been affected by several selection biases: In light of the advanced age of the study sample, a survivor bias might have influenced the study findings (Mayeda et al., 2016). The institutional group might have been particularly affected by the survivor bias, given the significantly different levels of CM between groups, coupled with the finding that higher rates of CM were previously linked to multiple health-impeding conditions and leading causes of death during adulthood (Felitti et al., 1998). Hence, individuals who did not participated may be less resilient. However, this cannot be confirmed as no complete

register currently exists for the deaths of individuals affected by CSMP in Switzerland (i.e., our sample of interest in the current study). Another selection bias may have affected the control group, indicated by the comparably high rates of reported exposure to CM (e.g., 38.5% physical abuse in the control group, compared to 81.9% in the institutional group; 33.6% sexual transgression in the control group, compared to 53.4% in the institutional group). This may be due to the fact that the study purpose was not blinded (i.e., recruitment study title: "Variability in responses to early-life adversity and their consequences on aging"), which might have led to a greater self-selection of participants with (higher rates of) CM experiences. Lastly, given the cross-sectional nature of this data, the present study could not consider the role of cumulative trauma and more recent trauma with regard to lifetime PTSD. It may be that participants would display variability with regard to the nature (e.g., subjective impact of the event, context of the event) and the sequence (e.g., duration, timepoint of occurrence in life) of such traumas. Therefore, a more sophisticated data collection with particular focus on the nature and sequence of traumatic events should be implemented in future studies to investigate and discuss the occurrence of cumulative trauma, recent trauma, and lifetime trauma in the aftermath of CM. Nevertheless, using a composite score of CM, the current study findings revealed important findings on CM and long-term correlates. Future studies may benefit from incorporating such a composite score with regard to traumatic events in the aftermath of CM. Despite the limitations, this study has several strengths as it examines the long-term correlates of CM experienced within an institutional context in an older adult sample (mean age of 70 years). This is important given the unique window of time in which to investigate this, due to the older age stages of the Swiss institutional sample. Insights gathered from this survivor population may help to foster intervention strategies for both current survivors and future generations affected by CM.

4.8 Conclusion

The present study showed that individuals from institutional contexts were exposed to higher levels of CM, reported higher rates of lifetime PTSD, and experienced less social acknowledgement compared to age-matched controls. However, the results also suggest that the level of CM exposure places individuals at a higher risk for the development of lifetime PTSD, over and above having been brought up in an institutional context. Therefore, to counteract the detrimental long-term consequences of CM and its association with lifetime PTSD, a critical issue for policy makers should be to enhance safeguarding measures against CM, not only within institutional contexts, but also in the general public. Furthermore, enhancing public education and awareness of the observed long-term correlates of CM, and institutional upbringing in particular, may help to foster understanding for affected individuals. This may in turn improve social acknowledgment towards survivors and support post-traumatic stress reduction.

5.2 Manuscript 2: Cognitive and Physical Functioning in Older Adults with a History of Welfare Care: Investigating the Mediating Role of Life Stressors

Carla M. Eising[1,2], Myriam V. Thoma[1,2], Manuel C. Voelkle[3], Viviane Pfluger[1,2], Andreas Maercker[1,2], & Shauna L. Rohner[1,2]

[1]University of Zürich, Psychopathology and Clinical Intervention, Institute of Psychology, Binzmühlestrasse 14/17, 8050 Zürich, Switzerland

[2]University Research Priority Program "Dynamics of Healthy Aging", University of Zürich, Zürich, Switzerland

[3]Humboldt University of Berlin, Rudower Chaussee 18, 12489 Berlin, Germany

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Abstract

Objectives: Early-life adversity (ELA), particularly within welfare contexts, can serve as an antecedent of health decline and heighten exposure to later-life stressors. However, research is lacking on the longer-term correlates of ELA in aging-relevant domains of cognitive and physical functioning. Therefore, this study aimed to investigate the long-term correlates of welfare-related ELA and cognitive and physical functioning in older adulthood. It further aimed to examine the potential mediating role of life stressors in this relationship.

Methods: A MANCOVA and mediation analysis were conducted with $N = 253$ older adults (n = 130 welfare group, mean age = 70.8; n = 123 age-matched controls, mean age = 70.7). Psychometric questionnaires and behavioral instruments assessed ELA, life stressors, and cognitive and physical functioning.

Results: Exposure to ELA was associated with lower subjective physical health. Furthermore, the welfare group showed lower general cognitive functioning and language comprehension, and more compromised subjective physical health and mobility in comparison to the control group. In the welfare group, the relationship between ELA and subjective physical health was significantly mediated by life stressors.

Discussion*:* The findings suggest that older adults with a history of welfare-related ELA may be more likely to experience life stressors, as well as reduced cognitive and physical functioning in later life. Future research and interventions aimed at the reduction of risk factors (i.e., life stressors) and these aging-relevant health domains may help to facilitate improvements in cognitive and physical functioning in this older adult population of welfare care survivors.

Keywords: Early-life adversity, life stressors, welfare care, cognitive and physical functioning

Cognitive and Physical Functioning in Older Adults with a History of Welfare Care: Investigating the Mediating Role of Life Stressors

1. Introduction

Early-life adversity (ELA), in the form of abuse or neglect in childhood or adolescence, has been linked to a range of negative health implications and is thought to serve as a risk factor for health decline throughout the lifespan (Bellis et al., 2019). For instance, research has shown an increased risk for significant health impairments following ELA, including mental health disorders, such as depression and anxiety (Rothrauff et al., 2009; Schrepf et al., 2014); as well as physical illnesses, such as cardiovascular disease and cancer (Dong et al., 2004; Keinan-Boker et al., 2009). However, the majority of these studies on the consequences of ELA have been conducted in younger to middle-aged adults, with a lack of research on the long-term health alterations in older age (Raposa et al., 2014; Robinaugh & McNally, 2011).

1.1 Early-Life Adversity in Welfare Care

When examining the long-term impact of ELA, an important sample in this emerging research area is those who have been affected by child welfare care. These individuals are often at higher risk for having experienced severe ELA (Lueger-Schuster et al., 2018). For instance, a recent large-scale review of international child welfare care found that these individuals were exposed to severe forms of emotional neglect (e.g., absence of a stable caregiver), physical neglect (e.g., malnutrition), emotional abuse (e.g., verbal abuse), physical abuse (e.g., hitting child with an object), and sexual abuse (e.g., indecent exposure) (Carr et al., 2020). Furthermore, research has demonstrated an association between child welfare care and lasting health consequences (Thoma et al., 2021a). For instance, a recent study with $N = 225$ middle-aged Scottish survivors (mean age = 59 years) showed that welfare care was associated with an increased risk for negative health outcomes, with 84% reporting mental health difficulties (e.g., depression) and

43% reporting physical health difficulties (e.g., frequent illness) (Carr et al., 2019). Such research suggests that individuals in welfare care may be affected by severe forms of ELA and hence may be more prone to significant health impairments. However, thus far, research with welfare care populations has largely focused on younger to middle-aged adults, with only little research studies examining the longer-term correlates in older adults.

1.2 Welfare Care and Cognitive and Physical Functioning

While some studies conducted with older adults have demonstrated associations between welfare-related ELA and psychological health and physical conditions (e.g., Carr et al., 2020; Thoma et al., 2021b), less research has focused on the long-term correlates with aging-relevant domains, such as cognitive functioning (e.g., general cognitive functioning, verbal fluency) or physical functioning (e.g., mobility, subjective physical health). Given the potential for age-related difficulties in cognitive and physical functioning (Christensen et al., 2013), this may be exacerbated in older populations with a history of ELA, and particularly welfare-related ELA, as many of these international welfare care cohorts are now reaching later-life stages (Carr, et al., 2020). With regard to cognitive functioning, a study was conducted with older Swiss former indentured child laborers (mean age = 78 years), a specific form of welfare placement in Switzerland. Results found that welfare-related ELA and subsequent post-traumatic stress symptoms were associated with general cognitive ability deficits in older age, as well as lower levels in specific cognitive domains, such as verbal numeracy and construction skills (Burri et al., 2013). While this study provides preliminary evidence for impaired cognitive functioning in individuals who experienced welfare-related ELA, the lack of a control group without welfare care experience limits the conclusions that can be drawn. Research is needed to investigate the long-term correlates of welfare-related ELA and cognitive functioning in older adults, with the inclusion of a control group (Aartsen et al., 2019).

In relation to physical functioning, welfare-related ELA has also been linked to physical health impairments in later life. Research within the same project as the current study showed that individuals with a history child welfare care reported more physical illnesses (e.g., diabetes, stroke) in comparison to an age-matched control group (Thoma et al., 2021b). However, this study focused on reported physical illness and health conditions and so research is still lacking on physical functionality in older adulthood. Some studies on general ELA (non-welfare-related) can provide an indication of the association between ELA and physical functionality. For example, a national US survey (N = 1,745; aged 25-84 years) showed that individuals with exposure to violence in childhood reported more health limitations in physical activities (e.g., carrying groceries), in comparison to individuals without such ELA (Greenfield & Marks, 2009). However, similar to research on cognitive functioning, there is a lack of studies specifically examining physical health and functioning in older individuals affected by welfare-related ELA, compared to age-matched controls.

1.3 ELA, Cognitive and Physical Functioning, and the Role of Life Stressors

With regard to the relationship between welfare-related ELA and cognitive and physical functioning, welfare-related ELA may not only have a direct effect, but factors following ELA may also influence outcomes. This is in line with the theory of cumulative disadvantage (Dannefer, 2003). More specifically, the theory of cumulative disadvantage proposes a systemic tendency towards interindividual divergence in a given characteristic across time (Dannefer, 2003). In applying this theory, it can be argued that welfare-related ELA may be associated with heightened exposure to future stressors or adversities over the life course. In support of this, a study on long-term correlates of welfare care in Austria found that adult survivors of welfare care reported a higher rate of exposure to traumatic life events in comparison to a community control group (Lueger-Schuster et al., 2018). With regard to

cognitive and physical functioning, research on general ELA (non-welfare-related) in a young-adult sample found that childhood trauma combined with recent stress was associated with poorer cognition (i.e., language processing, visuo-construction), compared to individuals without childhood trauma and healthy controls (Bücker et al., 2013). Similarly, a study on childhood abuse and adult health showed that childhood abuse combined with lifetime trauma exposure predicted physical and somatic symptoms in adulthood (Spertus et al., 2003). However, research is lacking in older adult samples on the role of life stressors in the relationship between welfare-related ELA and cognitive and physical functioning.

1.4 Research Gaps and Study Aims

The above research suggests that welfare-related ELA is associated with significant health consequences across the lifespan (Carr et al., 2019; Lueger-Schuster et al., 2018). However, there is a lack of research on welfare-related ELA and health outcomes in later life. Additionally, existing studies on the health correlates of welfare-related ELA have often focused on psychological disorders (e.g., depression) and health ailments (e.g., heart disease) (e.g., Carr et al., 2020; Lueger-Schuster et al., 2018). Thus, in older adult survivors of welfare-related ELA, research is needed to examine the aging-related domains of cognitive functioning (i.e., cognitive abilities, impairment) and physical functioning (i.e., mobility, subjective physical health, and functioning). Furthermore, given the potential for increased life stressors following welfare-related ELA (e.g., Dannefer, 2003; Bücker et al., 2013), there is a need to investigate this link in an older adult sample. To address these gaps in the literature, the current study aimed to investigate the link between welfare-related ELA, subsequent life stressors, and cognitive and physical functioning in older adulthood. In a first step, it was hypothesized that higher exposure to ELA would be related to lower cognitive and physical functioning as compared to lower ELA exposure. Furthermore, it was hypothesized that individuals affected

by welfare-related ELA would show lower cognitive and physical functioning in comparison to an age-matched control group. Finally, it was hypothesized that life stressors would mediate the relationship between ELA and cognitive and physical functioning in older adulthood, particularly for the welfare care group with high levels of ELA exposure.

2. Methods

2.1 Study Design and Context

The present study is embedded in the National Research Program "Welfare and Coercion – Past, present and future" (NRP76). The current data was collected within the project "*Differential aging trajectories in high-risk individuals with past experiences of early adversity*", from the baseline assessment conducted between July and December 2019. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the Faculty of Arts and Social Sciences in the University of Zürich (ID: 19.4.3).

2.2 Sample and Recruitment

General inclusion criteria were: aged 50 years and older and Swiss German speaking. Fifty was chosen as the cut-off in order to capture the various domains of age-related impairment (e.g., cognitive and physical health and functioning) while accounting for potential survivor bias (Mc Gee et al., 2018). The sample included two groups: (a) a welfare care group of individuals affected by welfare practices for at least one year in childhood and/or adolescence (up until 18 years old); and (b) an age-matched control group, not affected by welfare practices. Such welfare practices in Switzerland included forced child labor (i.e., the so-called former Verdingkinder; English: *contract children*) placement in foster homes (with and without forced labor), institutions (e.g., penal institutions), and psychiatric institutions, or forced medical

experiments and procedures (e.g., compulsory mediation, forced abortion, forced sterilization) (Federal Office of Justice, 2020). The reasons given for these welfare practices were often viewed as arbitrary. For instance, children and adolescents were often taken away if the parents were considered to live in a manner that conflicted with the social norms of that time, such as being a lone parent, having a mental illness, or living in considerable poverty (Leuenberger & Seglias, 2008).

The majority of the welfare care group were recruited via a list provided by the *Swiss Federal Office of Justice* (Federal Office of Justice, 2020). This list was compiled during the process for the solidary contribution, in which individuals indicated their willingness to participate in research studies that examined the subject of welfare practices in Switzerland. These individuals were sent an information letter, including the study aims, procedures, and contact information. Additional recruitment involved the use of posted flyers, newsletters, and the participant pool of the affiliated University Research Priority Program, *Dynamics of Healthy Aging* from University of Zürich.

2.3 Study Procedure

Individuals who were interested in participating called or emailed the study team using the contact information provided on the information letter and flyers. During the first contact, individuals were again informed about the study aims and procedure and were screened for the study inclusion criteria. If the criteria were met, two face-two-face appointments were scheduled, each lasting for a maximum of 120 minutes. The two appointments consisted of a structured clinical interview; questionnaires on ELA, welfare care, life stressors, and health; as well as physical and cognitive assessments. Following the completion of the two appointments, participants received a compensation of 240 Swiss Francs (approximately $250).

2.4 Measures

In addition to the self-report questionnaires and the cognitive and physical assessments, the following socio-demographic information were collected: age, gender, education, relationship status, satisfaction with financial status, and welfare-related information (i.e., age at first placement, type of welfare care, duration).

2.4.1 Early-Life Adversity and Life Stressors

ELA and adult life stressors were assessed using different subscales from the same instrument.

Traumatic Experience Checklist: ELA in childhood and/or adolescence was assessed with the German version of the Traumatic Experience Checklist (TEC; Nijenhuis et al., 2002). The TEC is a self-report inventory, composed of 29 items with varying Likert scales (e.g., presence of event: yes/no, impact of event: 5-point Likert scale). In accordance with the TEC scoring instructions (Nijenhuis et al., 2002), the following ELA scores were calculated: (1) Separate ELA types (emotional neglect, emotional abuse, physical abuse, sexual abuse), with each type including trauma exposure factors (e.g., presence of the event, age of onset, severity, type/variety, duration, and relationship with the perpetrator). (2) Total ELA exposure was then calculated by incorporating all ELA types and related trauma exposure factors. Higher scores on these scales indicate higher ELA exposure. Life stressors in adulthood (> 18 years) were also assessed with the TEC. A sum score was calculated for the presence of potential life stressors during adulthood, with a higher score indicating more life stressors. The German adaptation of the TEC has demonstrated a high criterion validity (e.g., in comparison with the Childhood Trauma Questionnaire) and high construct validity, shown by positive associations with posttraumatic stress, dissociation, anxiety, and depression symptoms (Schumacher et al., 2012). A Cronbach's alpha of $\alpha = .85$ to $\alpha = .94$ has been shown for the German version of the TEC (Schumacher et al., 2012). In the present sample, the Cronbach's alpha for ELA ranged from $\alpha = .58$ to $\alpha = .75$.

2.4.2 Cognitive Functioning

Two indicators of cognitive functioning were used to examine general cognitive performance and language comprehension/verbal intelligence.

Mini-Mental State Examination: The Mini-Mental State Examination (MMSE) was used as a screening tool for general cognitive functioning (Folstein et al., 1975). This includes tests of orientation, attention, memory, language, and visual-spatial skills. It yields a total score, with scores ranging from 0 to 30, with lower scores indicating worse cognitive functioning. A score of 24 or greater is considered to indicate "no cognitive impairment", a score between 18 to 24 indicates "mild cognitive impairment", and a score below 18 indicates "severe cognitive impairment" (Tombaugh & McIntyre, 1992). The MMSE has demonstrated good test-retest reliability of r = .90 (Pangman et al., 2000).

Wortschatztest [Vocabulary Test]: The 42-item German version of the Wortschatztest (WST) vocabulary test was used as an estimate of cognitive functioning with regard to language comprehension and verbal intelligence (Schmidt & Metzler, 1992). Raw values were transformed into a verbal intelligence quotient (IQ) scores using a norm value table. In the present study, the transformed scores ranged from 68 to 133. Higher scores indicate higher language comprehension and verbal intelligence. Following a Rasch scaling approach, the WST has demonstrated satisfactory reliability of α = .94 (Schmidt & Metzler, 1992).

2.4.3 Physical Functioning

Two indicators of physical functioning were used to examine subjective physical health and mobility.

Short-Form Health Survey Version 2: The physical component summary (PCS) of the German Short-Form Health Survey Version 2 (SF-36 V2) was used to assess subjective physical health (Bullinger, et al., 1995; Morfeld et al., 2005). The PCS is a weighted composite score that encompasses eight subscales: physical functioning, role physical, bodily pain, general health,

vitality, social functioning, role emotional, and emotional well-being. Higher scores indicate higher levels of self-reported physical health. The scale has shown good test-retest reliability ($r > .80$) in older adult populations (Haywood et al., 2005). In the present sample, the SF-36 subscales used to calculate the PCS score showed good Cronbach's alphas: physical functioning: $\alpha = .93$, role physical: $\alpha = .89$, bodily pain: $\alpha = .87$, general health: $\alpha = .76$, vitality: $\alpha = .87$, social functioning: $\alpha = .84$, role emotional: $\alpha = .84$, emotional well-being: $\alpha = .87$.

Timed "Up and Go": The Timed "Up and Go" (TUG) was used to assess physical functioning in relation to mobility, i.e., mobility and balance impairment (Podsiadlo & Richardson, 1991). This assessment requires participants to rise from a chair and walk three meters at a comfortable pace to a marked position on the floor and then return to the chair in a seated position. It yields a single score, comprised of the time (in seconds) that it takes to complete the task. Scores are sorted into five categories, which were used in the present study: 1) under 10 seconds, 2) 10-19 seconds, 3) 20-29 seconds, 4) 30 or more seconds, 5) unable to walk. Lower categories (i.e., quicker times) indicate better mobility. The TUG has demonstrated good reliability with a Cronbach's alpha of $\alpha = .70$ to .90 (Van Lummel et al., 2016).

2.5 Data Analysis

Statistical analyses were performed using the IBM Statistical Package for Social Sciences (SPSS) version 25.0 and the macro-PROCESS version 3.0 (IBM Corp., Armonk, N.Y., USA, 2017; Hayes, 2018). Less than 1% missing values were observed for all instruments. Little's missing completely at random (MCAR) indicated that missings were MCAR and were replaced with the Expectation-Maximization algorithm (Dempster et al., 1977; Little, 1988). Furthermore, data was missing on an instrument level for $n = 12$ participants on the WST, $n = 7$ on the TUG, and $n = 4$ on the MMSE, and the respective analyses were conducted using only complete data for each instrument. In a first step, to examine if total ELA exposure was

associated with cognitive and physical functioning, four linear regression analyses were performed for each of the outcome variables (MMSE, WST, PCS, TUG), while controlling for socio-demographic covariates (age, gender, education, relationship status, and satisfaction with financial status). In a second step, multivariate regression analyses were performed to investigate if certain types of ELA were associated with differences in cognitive and physical functioning. Furthermore, to examine group differences in cognitive and physical functioning between the welfare care group and matched control group, a multivariate analysis of co-variance (MANCOVA) was conducted (covariates: total ELA exposure and socio-demographic variables: age, gender, education, relationship status, and satisfaction with financial status). To examine the potential mediating role of life stressors on the relationship between ELA and cognitive and physical functioning, mediation analyses (model 4) were conducted for the welfare care group and the control group (Hayes, 2018). Confidence intervals in the mediation analyses were calculated using bootstrapping (number of bootstrap samples = 5000) following the guidelines of Shrout and Bolger (2002).

3. Results

3.1 Sample Characteristics

A total of N = 257 participants were recruited (n = 132 welfare care group, n = 125 control group). From this, two participants in the welfare care group dropped out during the baseline assessment and two participants from the control group were excluded due to complete missing data on the TEC. The final sample consisted of N = 253 participants (n = 130 welfare care group, mean age = 70.8 years, SD = 12.4; n = 123 control group, mean age = 70.7 years, SD = 9.6). In the welfare care group 41.5% (n = 54) were female and in the control group 50.4% (n = 62) were female. Regarding education, the majority of the welfare care group completed vocational training (43.8%), whereas the majority of the control group (38.2%) had a university

degree (see Table 8 for the sample characteristics). On average, participants in the welfare care group were 5.6 years old (*SD* = 4.4) when they entered welfare care and spent, on average, 11.4 years (*SD* = 5.8) in welfare care (ranging from less than one year to 19 years). Regarding the type of welfare care, 48.7% of the welfare care group were affected by forced child labor, either in a foster family or a care home for children. Other welfare care included compulsory adoption (8%), and placement in penal institutions (5.3%) and psychiatric institutes (3%).

Table 8

Sample Characteristics

Sample Characteristics	Total Sample (N = 253)			Welfare Care Group (n = 130)			Control Group (n = 123)			Group Comparisons
	Total	Male	Female	Total	Male	Female	Total	Male	Female	p
M_{age}	70.7	71.0	70.5	70.8	71.1	70.4	70.7	70.8	70.6	p = .939
Education										X^2 = 49.22, p < .001***
No education	6 (2.4)	3 (2.2)	3 (2.6)	6 (4.6)	3 (3.9)	3 (5.6)	0 (0)	0 (0)	0 (0)	
Primary school	10 (4.0)	4 (2.9)	6 (5.2)	9 (6.9)	4 (5.3)	5 (9.3)	1 (0.8)	0 (0)	1 (1.6)	
Upper secondary school	26 (10.3)	14 (10.2)	12 (10.3)	21 (16.2)	13 (17.1)	8 (14.8)	5 (4.1)	1 (1.6)	4 (6.5)	
High school	6 (2.4)	1 (0.7)	5 (4.3)	2 (1.5)	0 (0)	2 (3.7)	4 (3.3)	1 (1.6)	3 (4.8)	
Vocational job training	99 (39.1)	47 (36.5)	49 (42.2)	57 (43.8)	34 (44.7)	23 (42.6)	42 (34.1)	16 (26.2)	26 (41.9)	
Higher professional training	37 (14.6)	24 (17.5)	13 (11.2)	18 (13.8)	14 (18.4)	4 (7.4)	19 (15.4)	10 (16.4)	9 (14.5)	
University	56 (22.1)	36 (26.3)	20 (17.2)	9 (6.9)	5 (6.6)	4 (7.4)	47 (38.2)	31 (50.8)	16 (25.8)	
Other	13 (5.1)	5 (3.6)	8 (6.9)	8 (6.2)	3 (3.9)	4 (7.4)	5 (4.1)	2 (3.3)	3 (4.8)	

Sample Characteristics	Total Sample (N = 253)			Welfare Care Group (n = 130)			Control Group (n = 123)			Group Comparisons
Relationship status										X^2 = 7.29, p = .200
Single	31 (12.3)	15 (10.9)	16 (13.8)	17 (13.1)	11 (14.5)	6 (11.1)	14 (11.4)	4 (6.6)	10 (16.1)	
Relationship	29 (11.5)	16 (11.7)	13 (11.2)	16 (12.3)	10 (13.2)	6 (11.1)	13 (10.6)	6 (9.8)	7 (11.3)	
Married	106 (41.9)	79 (57.7)	27 (23.3)	47 (36.2)	37 (48.7)	10 (18.5)	59 (48.0)	42 (68.9)	17 (27.4)	
Separated	5 (2.0)	5 (3.6)	0 (0)	4 (3.1)	4 (5.3)	0 (0)	1 (.8)	1 (1.6)	0 (0)	
Divorced	49 (19.4)	15 (10.9)	34 (29.3)	31 (23.8)	11 (14.5)	20 (37.0)	18 (14.6)	4 (6.6)	14 (22.6)	
Widowed	33 (13.0)	7 (5.1)	26 (22.4)	15 (11.5)	3 (3.9)	12 (22.2)	18 (14.6)	4 (6.6)	14 (22.6)	
Satisfaction with finance										X^2 = 29.87, p < .001***
Very dissatisfied	28 (11.1)	2 (1.5)	7 (5.7)	21 (16.2)	1 (1.3)	7 (13.0)	7 (5.7)	5 (8.2)	2 (3.2)	
Dissatisfied	48 (19.0)	21 (16.2)	15 (12.2)	33 (25.4)	14 (18.4)	12 (22.2)	15 (12.2)	6 (9.8)	9 (14.5)	
Satisfied	16 (45.8)	33 (25.4)	57 (46.3)	59 (45.4)	21 (27.6)	29 (53.7)	57 (46.3)	29 (47.5)	28 (45.2)	
Very Satisfied	59 (23.3)	59 (45.4)	44 (35.8)	15 (11.5)	30 (39.5)	5 (9.3)	44 (35.8)	21 (34.4)	23 (27.1)	

Note. M_{age} = mean age in years, X^2 = Chi-square test, p = p-value, ** p <.05, *** p < .001.

3.2 Early-life Adversity and Cognitive Functioning

In the first step, total ELA exposure significantly predicted cognitive functioning, as measured by the WST (F (1, 239) = 4.79, p = .030). However, after including the covariates (age, gender, education, relationship status, and satisfaction with financial status), total ELA exposure was no longer a significant predictor (p = .104). The model including covariates explained 19.4% of the variance in WST, with level of education being the strongest predictor of WST performance (p < .001). In the multivariate regression (incorporating all ELA types) no ELA type was shown to significantly predict WST performance (F (1, 236) = 1.72, p = .147). ELA (total exposure or any ELA type) did not significantly predict general cognitive functioning, as measured by the MMSE (p > .05). See Table 9 for the regression analyses for cognitive functioning.

3.3 Early-life Adversity and Physical Health and Mobility

Total ELA exposure significantly predicted subjective physical health, as measured by the PCS (F (1,251) = 14.67, p < .001). After including the covariates (age, gender, education, relationship status, and satisfaction with financial status), total ELA exposure remained a significant predictor (F (1,246) = 6.27, p < .001). This model explained 13.3% of the variance in PCS, with total ELA exposure (p < .001) and level of education (p < .001) being the only significant predictors. In the multivariate regression (incorporating all ELA types) emotional neglect (p = .010), physical abuse (p = .037), and sexual abuse (p = .044) significantly predicted subjective physical health, as measured by the PCS (F (1,243) = 4.78, p < .001). ELA (total exposure or any ELA type) did not significantly predict mobility, as measured by the TUG (p > .05). See Table 9 for the regression analyses for subjective physical functioning.

Table 9

Regression Analysis of Early-Life Adversity, Verbal Intelligence, and Subjective Physical Health

Variable	R^2	***F***	***b***	***p***
Cognitive functioning (WST)				
Total ELA exposure	.02	4.79	-.11	p = .030**
Analysis with covariates	.19	9.36		p < .001 ***
Total ELA exposure			-.08	p = .104
Gender			-.36	p = .808
Age			.07	p = .321
Relationship status			-.26	p = .603
Education			3.16	p < .001 ***
SES			-.01	p = .905
Physical functioning (PCS)				
Total ELA exposure	.06	14.67	-.18	p < .001 ***
Analysis with covariates	.13	6.27		p < .001 ***
Total ELA exposure			-.20	p < .001 ***
Gender			1.49	p = .283
Age			-.10	p = .112
Relationship status			-.58	p = .204
Education			1.63	p < .001 ***
SES			.01	p = .849

Note. b = regression coefficient, R^2 = goodness-of-fit measure, F = difference in variance, WST = Wortschatztest/vocabulary test, PCS = physical component score, SES= socio-economic status, p = p-value, ** p <.05, *** p < .001.

3.4 Group Differences in Cognitive and Physical Functioning

Results of the MANCOVA showed that the welfare care and control groups significantly differed in the cognitive and physical functioning outcomes (F (1, 239) = 16.85, $p < .001$; Wilk's $\Lambda = .77$, partial $\eta^2 = .23$). In comparison to the control group, the welfare care group showed significantly lower WST performance (welfare care group: $M = 101.0$, $SD = 11.0$; control group: $M = 113.8$, $SD = 9.5$), significantly lower general cognitive functioning (MMSE; welfare care group: $M = 27.7$, $SD = 1.7$; control group: $M = 28.6$, $SD = 1.5$), significantly lower subjective physical health (PCS; welfare care group: $M = 46.1$, $SD = 11.2$; control group: $M = 54.8$, $SD = 9.6$), and significantly lower mobility (TUG; welfare care group: $M = 1.6$, $SD = .8$; control group: $M = 1.3$, $SD = .7$). See Table 10 for the MANCOVA results.

Table 10

Multivariate Analysis of Co-Variance of Cognitive and Physical Functioning

Dependent variable	*df*	*F*	*p*	Eta^2	Welfare Care Group		Control Group	
Cognitive functioning					*M*	*SD*	*M*	*SD*
WST	1, 241	57.29	$p < .001$ ***	.19	101.0	11.0	113.8	9.5
MMSE	1, 249	6.97	$p = .009$ **	.03	27.7	1.7	28.6	1.5
Physical functioning								
PCS	1, 253	18.40	$p < .001$ ***	.07	46.1	11.2	54.8	9.6
TUG	1, 246	4.15	$p = .043$ **	.02	1.6	.8	1.3	.7

Note. df = degrees of freedom, F = F-value, Eta^2 = effect size, M = mean, SD = standard deviation, WST = Wortschatztest/vocabulary test, MMSE = Mini-Mental State Examination, PCS = physical health component score, TUG = Timed "Up and Go", p = p-value, ** $p < .05$, *** $p < .001$.

3.5 Life Stressors as a Mediator

The relationships between ELA and cognitive and physical functioing in the welfare care and the control groups were further explored through mediation analyses investigating life stressors as a mediator. With regard to cognitive functioning, life stressors did not significantly mediate the relationship between ELA and any indicator of cognitive functioning (WST, MMSE) in either the welfare care or control groups.

With regard to physical functioning, life stressors significantly mediated the relationship between total ELA exposure and subjective physical health (PCS) in the welfare care group (see Figure 3). A significant positive association was observed (b = .09, SD = .02, p < .001), indicating that those with higher levels of total ELA exposure were more likely to have experienced more life stressors. A significant negative association was observed between life stressors and physical health (b = -1.25, SD = .36, p < .001), indicating that those with more life stressors showed worse subjective physical health (PCS). A significant negative total effect was observed between total ELA exposure and subjective physical health (PCS) (b = -0.16, 95% CI [-.316, -.002], t = -2.02, p = .046), explaining 3.6% of the variance in physical health. When life stressors were included as a mediator, a significant indirect effect was observed (b = -.11, 95% CI [-.21, -.04]), indicating that life stressors significantly mediated the relationship between total ELA exposure and subjective physical health (PCS), explaining 13.1% of the variance. With regard to the control group, life stressors did not significantly mediate the relationship between ELA or any indicator of physical functioning (PCS, TUG).

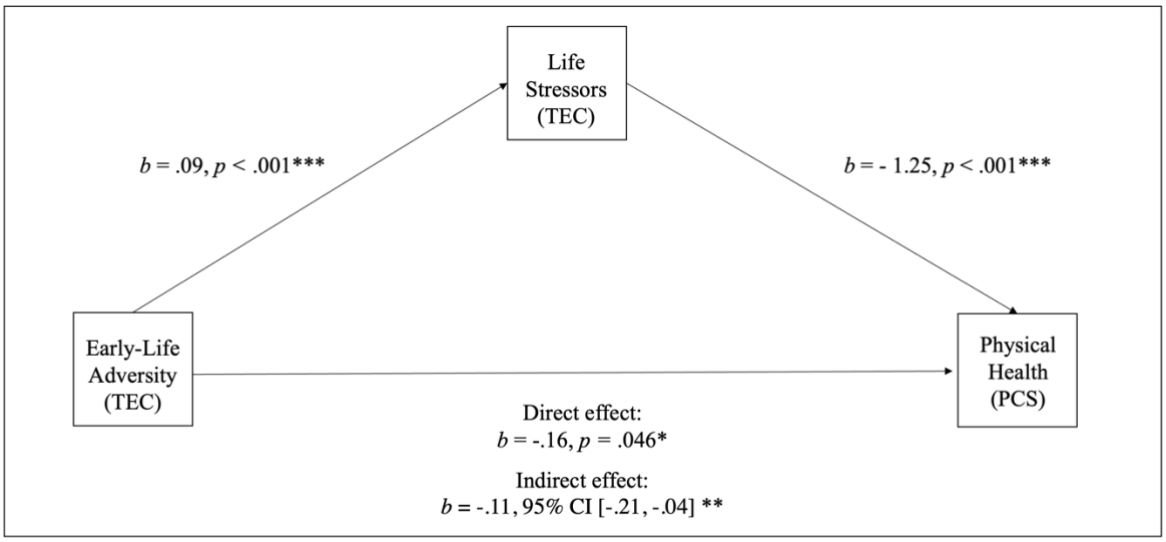

Figure 3. Mediation model in the welfare care group of the relationship between early-life adversity (predictor) and subjective physical health (outcome variable), mediated by life stressors.

4. Discussion

The current study examined the link between welfare-related ELA, life stressors, and cognitive and physical functioning in older age. Results showed that total ELA exposure did not predict lower levels of cognitive functioning, but significantly predicted lower levels of physical functioning. With regard to group differences, individuals with a history of welfare care showed significantly lower cognitive and physical functioning compared to individuals in the control group. Further investigations of this finding revealed that in the welfare care group, the relationship between total ELA exposure and physical health was significantly mediated by life stressors.

Regarding cognitive functioning, total ELA exposure was not shown to impact cognitive functioning in older adulthood in the present study. This contrasts with findings on ELA and cognitive functioning in young to middle-aged adults. For instance, in a study with

individuals aged 19-46 years, those with a history of childhood abuse had significantly lower verbal intelligence scores in comparison to individuals with no childhood abuse (Bae et al., 2010). Regarding general cognitive functioning, a study with adults aged 18-45 years showed that ELA was associated with cognitive deficits in a global assessment of memory and executive functioning (Gould et al., 2012). One explanation for present findings may be that in an older population, other aging-related factors (e.g., physical inactivity, social engagement) or socio-demographic factors (e.g., education, socio-economic status) may have a bigger influence on cognitive functioning in older age than ELA exposure. In support of this, education was observed in the present study to be the strongest predictor of cognitive functioning, over and above ELA.

With regard to physical functioning, the present results showed that total ELA exposure predicted lower subjective physical health, which adds support to previous research on health conditions and ailments. For example, a large study on health consequences of child maltreatment in individuals aged between 25 and 74 years showed that those with a history of child maltreatment reported worse physical health (i.e., higher number of chronic medical conditions) compared to non-maltreated individuals (Schafer et al., 2013). Furthermore, results of the present study on ELA type showed that emotional neglect and physical and sexual abuse were linked to lower subjective physical health in older adulthood. This is consistent with the existing literature on ELA. For example, in a national cross-sectional health survey, child abuse (e.g., physical and sexual) was related to poor self-perceived health and physical conditions in a dose-response manner (Afifi et al., 2016). However, in contrast to previous studies, the present results did not observe an association between ELA and mobility in older adulthood. For instance, a large study on childhood abuse and later-life mobility (aged 65-74 years) found that exposure to physical violence in childhood was associated with mobility disability (i.e., limitations in walking) in later life (Guedes et al., 2016). It may be that the current findings

highlight important differences between subjective physical health and objective assessments of mobility. Subjective physical health may not only depict functional status, but may also reflect related perceptions of health, life satisfaction, and external resources (Araujo et al., 2018). It may be that such complex subjective impairments can impact older adult's health and well-being before objective mobility decline is evident. To better understand the link between ELA and all aspects of physical functioning in later life, future studies should assess a variety of subjective and objective health indicators in older adult samples.

Regarding the comparison of the welfare care and control groups, individuals with a history of welfare care showed lower cognitive and physical functioning in comparison to the control group, and with meaningful effect sizes. By examining cognitive and physical functioning in older adulthood, the current study expanded upon existing studies on ELA and welfare care, which have predominantly focused on psychological disorders and physical ailments or conditions (e.g., Carr et al. 2020; Lueger-Schuster et al., 2018). Additionally, the current study expanded on the existing literature by examining life stressors as a potential mediating factor in the relationship between ELA and cognitive and physical functioning. Meaningful differences emerged between the welfare care and control groups, with life stressors significantly mediating the relationship between total ELA exposure and subjective physical health in the welfare care group, but not the control group. Consistent with the theory of cumulative disadvantage (Dannefer, 2003), these findings suggest that individuals with a heightened exposure to adversity in childhood or adolescence are more likely to experience an increased number of life stressors over the life course (McLaughlin et al., 2010; Hammen et al., 2000). This finding is also in line with the limited research on welfare care and subsequent traumatic life events. For example, a study on long-term correlates of institutional abuse in participants aged 29-87 years found that individuals exposed to ELA during welfare care reported an increased exposure to traumatic life events in comparison to a community control

group (Lueger-Schuster et al., 2018). Given the increased risk for later life stressors in welfare care samples, future research should also examine potential moderating factors (e.g., education, access to services) that could reduce the risk of further stressors and potentially buffer the negative impact of ELA on later-life health and functioning.

A number of limitations of the current study must be considered, which can help identify avenues for further research. First, given the cross-sectional design of the current study, conclusions about causal inferences cannot be made. Future research should aim to replicate this study using a longitudinal research design. Second, ELA was assessed using a retrospective self-report measure, which may be subject to recall bias, particularly in an older adult sample (McPhail & Haines, 2010). However, the current study sample included a unique population of individuals affected by historic (welfare care) practices, for which a prospective study design would not have been possible. Third, the welfare care group may have been affected by sampling bias or survivor bias. It is estimated that tens of thousands of individuals were affected by such welfare practices in Switzerland with only about 12,000 to 15,000 individuals still alive today (Federal Office of Justice, 2020). Therefore, it may be that in this specific aging population, those who choose to participate in research on this topic may be generally healthier. Of those, an even smaller minority may be willing to disclose their childhood experiences. However, this is a unique window of opportunity in which to study this population of older individuals with a history of welfare upbringing. The findings of the current study are also of international interest, as similar welfare practices have occurred in several international cohorts who are also now reaching older age stages, such as in Ireland (Carr et al., 2020; Fitzpatrick et al., 2010) and Austria (Lueger-Schuster et al., 2018). Furthermore, research on long-term health outcomes in older populations is of utmost importance, particularly in the aging-relevant domains of cognitive and physical functioning, in light of the general shift towards an aging society with an increased number of individuals living longer lives (WHO, 2015). This

population aging poses challenges to health and social care services in the treatment of older individuals (Baltes & Smith, 2003). Thus, research is urgently needed to address health and disability in later life, particularly in such ELA populations with the potential for significant health impairments.

In conclusion, the results of the current study showed that regardless of group, ELA was linked to lower physical, but not cognitive, functioning in older age. Decreased subjective physical health was particularly evident in the welfare care group, which was mediated by high rates of life stressors. Overall, this study has shown that older adults with a history of welfare-related ELA may be more likely to experience life stressors, as well as reduced cognitive and physical functioning in later life. Future research and interventions aimed at these aging-relevant health domains, as well as the reduction of risk factors (i.e., life stressors), may help to facilitate improvements in cognitive and physical functioning in this older adult population of welfare care survivors.

5.3 Manuscript 3: A Longitudinal Resting-state Functional Connectivity Analysis on Trauma Exposure and Post-traumatic Stress Symptoms in Older Individuals

Carla M. Eising[1,2*], Andreas Maercker[1,2], Brigitta Malagurski[2,], Lutz Jäncke[2,3] and Susan Mérillat[2]

[1]University of Zürich, Psychopathology and Clinical Intervention, Institute of Psychology, Binzmuehlestrasse 14 / 17, 8050 Zürich, Switzerland

[2]University Research Priority Program "Dynamics of Healthy Aging", University of Zürich, Switzerland

[3]Division Neuropsychology, Department of Psychology, University of Zurich, Switzerland

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Abstract

Background: Given the present demographic shift towards an aging society, there is an increased need to investigate the brain's functional connectivity in the context of aging. Trauma exposure and post-traumatic stress disorder (PTSD) symptoms are factors known to impact healthy aging and have been reported to be associated with functional connectivity differences. In the present study, we examined and compared differences in with-Default Mode Network (DMN), within-Salience Network (SN) and between DMN-SN functional connectivity between trauma-exposed individuals with and without PTSD symptoms as well as non-trauma-exposed individuals in a non-clininical older adult sample.

Methods: Resting-state fMRI and behavioral data is drawn from the Longitudinal Healthy Aging Brain Database Project (LHAB). For the present analysis, participants who completed the questionnaires on trauma exposure and PTSD symptoms ($N = 110$; mean age = 70.55 years, $SD = 4.82$) were included.

Results: On on a trend level, the reporting of PTSD symptoms relative to no symptoms was associated lower within-DMN connectivity, while trauma-exposed individuals showed higher within-SN connectivity compared to non-trauma exposed individuals. Consistent with existing models of healthy aging, between DMN-SN functional connectivity showed an increase across time in older age.

Conclusion: Present results suggest that alterations in within-DMN and within-SN functional connectivity also occur in non-treatment seeking older adult populations following trauma exposure and in association with PTSD symptoms and manifest besides altered between DMN-SN functional connectivity in older age supposingly independent of aging-related functional dedifferentiation.

Keywords: rs-fMRI, post-traumatic stress symptoms, trauma exposure, aging, functional connectivity

A Longitudinal Resting-state Functional Connectivity Analysis on Trauma Exposure and Post-traumatic Stress Symptoms in Older Individuals

Introduction

During the past years there has been a growing interest in investigating intrinsic connectivity networks (ICN) to study the brain's intrinsic organization across different brain developmental stages (Damoiseaux, 2017; Sullivan et al., 2019; Qiao et al., 2019). Within the context of aging, it is suggested that the organization of the brain's ICN changes as a function of aging. From pertinent studies, of which most are cross-sectional in nature, evidence was derived for lower functional connectivity within several ICNs (e.g., default mode, frontoparietal control and salience ventral attention network) and higher functional connectivity between networks in older as compared to younger adults – a pattern that has been termed as functional dedifferentiation (Jockwitz & Caspers, 2021; Malagurski et al., 2020; Setton et al., 2021). Given the stated ICNs association with aging and the fact that more and more adults reach later life stages (Fuster, 2017; Phillips & Razak, 2021), it is of outmost importance to further our understanding on how the brain's intrinsic organization changes by age and which factors may have an impact on differential aging trajectories.

One factor that is thought to meaningfully influence aging trajectories with respect to intrinsic connectivity is the exposure to current or past traumatic events (Cook & Simiola, 2018). So far, however, the majority of research on trauma exposure has been conducted in adolescence and young to middle aged adults (López et al., 2017; Sowder et al., 2018) and there exists only ample evidence for long(er)-term health and brain functioning outcomes following trauma exposure in older age (Reuveni et al., 2016; Szeszko & Yehuda, 2019). Hence, an interesting path to follow is the investigation of trauma exposure in older individuals, who may have also had a higher chance of having been exposed to traumatic events in their earlier life (Glaesmer et al., 2010). This is further of interest since post-traumatic stress disorder (PTSD) symptoms,

as the most prevalent subsequent psychopathology, may manifest differently in older adults (Maercker, 2021). More precisely, epidemiological studies have shown that the prevalence of past year PTSD is significantly lower for older adults as compared to younger and middle-aged adults and is most likely to unfold in a subthreshold representation of PTSD symptoms (de Vries & Olff, 2009; Reynolds et al., 2016). Although not meeting full diagnostic criteria for PTSD, older individuals' health and brain functioning may still be meaningfully affected by symptoms on a subthreshold syndromale level (Pietrzak et al., 2012). Hence, there is much to suggest to also thoroughly examine the impact of trauma exposure and PTSD symptoms on ICNs in non-clinical older adult populations.

Up until now, our understanding of ICNs in trauma-exposed individuals and PTSD symptoms is primarily based on studies using clinical populations. On the basis of resting-state functional Magnetic Resonance Imaging (rs-fMRI), a method that is commonly used to measure resting-state functional connectivity (rs-FC) within and between ICNs, differences between trauma-exposed individuals with and without PTSD within and between ICNs (Fu et al., 2019; Garrett et al., 2019; Misaki, et al., 2018) have been revealed. More precisely, two ICNs have been of particular interest in this area of research: a) the default mode network (DMN), implicated in internally directed cognition (Buckner et al., 2019), and b) the salience network (SN), responsible for evaluating the valence of incoming stimuli (Uddin, 2015). However, so far no consensus exists whether the brain's intrinsic connectivity patterns are sensitive to trauma exposure per se or if changes in ICNs are related to the presence of PTSD symptoms.

For instance, in a study adressing consequences of early-life trauma, individuals suffering from chronic PTSD showed lower within-DMN rs-FC compared to non-trauma exposed controls (Bluhm et al., 2009). Other studies compared trauma-exposued individuals with and without PTSD to non-trauma exposed controls. Whilst one study observed reduced within-DMN rs-FC in individuals with trauma-exposure with and without PTSD compared to non-traumatized

controls (DiGangi et al., 2016), another study observed lower within-DMN rs-FC in individuals reporting PTSD as compared to non-trauma exposed controls, but no differences between trauma-exposed individuals and non-trauma exposed controls (Sheynin et al., 2020), suggesting abbarrent within-DMN rs-FC predominantly in individuals with PTSD symptoms.

In the same vein, previous research findings declare the SN to be hyperconnected in PTSD and/or trauma-exposed individuals (Sripada et al., 2012). However, here differences in the brain's intrinsic organization are thought to stem from a different course of action. More precisely, previous studies have shown that individuals with prior trauma exposure (with or without PTSD symptoms) display greater within-SN rs-FC as compared to non-trauma exposed controls (Chen et al., 2019; Sheynin et al., 2020; Stark et al., 2015), translating into the assumption that trauma exposure alone and not the manifestation of PTSD symptoms contributes to abbarent within-SN rs-FC.

Additionally, there are mixed findings with regard to between between-network (DMN-SN) rs-FC. While in some studies individuals with PTSD exhibited greater cross-network functional connectivity between DMN and SN in comparison to non-trauma exposed controls (Block et al., 2017; Sripada et al., 2012; Zhang et al., 2015), another study observed lower connectivity between the DMN and attentional control networks in individuals with PTSD (Patriat et al., 2016). Further, when comparing trauma-exposed individuals with and without PTSD and non-trauma exposed individuals, only those suffering from PTSD and neither trauma-exposed nor non-trauma exposed individuals showed DMN-SN desegregation (Sheynin et al., 2020). Hence in order to improve our understanding regarding ICN changes following trauma exposure and the neurogenesis of PTSD a threefold group differentiation (e.g., individuals with PTSD, trauma-exposed individuals without PTSD and non-trauma exposed controls), may be crucial in future investigations (Abdallah et al., 2019; Sripada et al., 2012).

Beyond the levels of within- and between-network rs-FC, our knowledge is very limited when it comes to the question whether true within-person change of rs-FC is affected by trauma exposure or PTSD symptoms. Most of the research has been cross-sectional and longitudinal studies have primarily been conducted to measure functional abnormalities prior and post PTSD therapy (Zhou et al., 2012). To the best of our knowledge, there have not been any published longitudinal rs-FC studies on trauma exposure and PTSD symptom-related changes in a non-clinical older adult sample (> 65 years).

As such, our aim, which was also preregistered prior to performing any analysis (link to preregistration will be added after review), was to investigate and compare rs-FC within and between ICNs as well as longitudinal change in these metrics in non-clinical older individuals (a) with prior trauma exposure and PTSD symptoms, (b) with prior trauma experience but no PTSD symptoms and (c) with no trauma exposure. We hypothesized that, in the present non-clinical sample, individuals with prior trauma exposure compared to non-trauma exposed individuals, a) display greater within-SN connectivity but do not show aberrant within-DMN or between-network connectivity, and b) display greater enhancement of within-SN connectivity across time but not with regard to within-DMN or between-network connectivity. Further, we hypothesize that individuals with PTSD symptoms compared to those without, c) show weaker within-DMN connectivity, stronger within-SN and greater between DMN-SN connectivity, and d) display decline of within-DMN connectivity across time as well as an enhancement of within-SN and between DMN-SN connectivity across time.

Methods

Participants

Data from five measurement occasions (i.e., baseline, 1-year follow-up, 2-year follow-up, 4-year follow-up, 7-year follow-up) were taken from the Longitudinal Healthy Aging Brain

Database Project (LHAB; Switzerland) conducted at the University of Zürich (Zöllig et al., 2011). At each measurement, participants underwent brain imaging, performed a battery of psychometric cognitive and motor ability tests and completed different questionnaires. The inclusion criteria at baseline were a minimum age of 64, right-handedness, fluent German language proficiency. Participants with a history of neurological diseases of the central nervous system, contraindications to MRI and a score of below 26 on the Mini Mental State Examination (MMSE; Folstein et al., 1975) were excluded. The study was approved by the ethical committee of the canton of Zürich and all participants gave informed consent in accordance with the declaration of Helsinki.

For the present analysis, only participants who completed questionnaires on trauma exposure and PTSD symptoms, which were administered at the 4-year follow-up occasion, were included, resulting in a sample of N = 110 individuals of which n = 50 individuals reported previous trauma exposure and n = 25 individuals reported PTSD symptoms. The full sample (including individuals with and without trauma exposure) had a mean age of 70.55 years (SD = 4.82) with 50% of the sample being female (n = 55). The level of education was assessed on a scale from 1 to 3; 1 = high school with or without vocational education (N = 33), 2 = higher education entrance qualification, business school or university of applied sciences (N = 22), or 3 = university degree (N = 55). Further socio-demographic information are displayed in Table 11.

Table 11

Sample Characteristics

Variable	Entire sample (N = 110)	Individuals with trauma exposure (n = 50)	Individuals with PTSD symptoms (n = 25)
M_{age} (*SD)*	70.55 (*4.82*)	70.89 (4.96)	71.26 (5.05)
Sex *n* (%)			
Female	55 (50)	28 (56)	13 (52)
Male	55 (50)	22 (44)	12 (48)
Education *n* (%)			
High school	33 (30)	14 (28)	6 (24)
Higher education	22 (20)	11 (22)	7 (28)
University degree	55 (50)	25 (50)	12 (48)

Note. M_{age} = mean age, *SD* = standard deviation, *N/n* = number of individuals, PTSD symptoms = individuals with post-traumatics stress disorder symptoms.

Trauma Exposure and Post-Traumatic Stress Measure

The 7-item Short Screening Scale for DSM-IV Posttraumatic Stress Disorder (Breslau et al., 1999; Siegrist & Maercker, 2010) was used to screen for trauma exposure over the life course and presence of PTSD symptoms within the last months. The inventory measures the frequencies of seven PTSD symptoms within the last months: intrusions, flashbacks, nightmares, avoidance internal, avoidance external, hypervigilance and exaggerated startle response. Regarding trauma exposure, a total of eight different types of traumatic events were assessed using the trauma exposure items of the DIA-X interview (Wittchen & Pfister, 1997): war experience, physical abuse, sexual abuse, sexual abuse in childhood, natural disaster, serious accident, imprisonment, witness of a traumatic event. Regarding the frequency of exposure to a traumatic event and the distribution of PTSD symptoms: a total of n = 60 individuals reported to not have been expoed to a traumatic event, while n = 50 individuals

reported that they have been exposed to at least one traumatic event in their lives. For the symptom prevalence, of the *n* = 25 individuals reporting PTSD symptoms, *n* = 17 (68%) reported intrusions, *n* = 10 (40%) nightmares, *n* = 10 (40%) flashbacks, 11 (44%) internal avoidance, *n* = 6 (24%) external avoidance, *n* = 5 (20%) hypervigliance when reminded and *n* = 7 (28%) exaggerated startle response.

MRI Acquisition

MRI scanning was performed on a Philips 3 T Ingenia Medical Scanner with a 32-channel head coil and comprised T1-weighted anatomical scans (160 slices; TR 1⁄4 8.1 ms, TE 1⁄4 3.7 ms, FOV 1⁄4 240 x 240, 160 mm, flip angle 1⁄4 8º, isotropic voxel size 1⁄4 1.0 1.0 1.0 mm3) and T2* weighted rs-fMRI scans (gradient echo-planar sequence; transverse slice orientation; 43 slices; voxel size: 3.5 x 3.5 3.5 mm3; TR 1⁄4 2000 ms; TE 1⁄4 21 ms; flip angle 1⁄4 76º; FOV 1⁄4 220 x 220 150 mm). For the rs-fMRI scan, participants were instructed to lie relaxed, while keeping their eyes open.

MRI Preprocessing

Results included in this manuscript come from preprocessing performed using FMRIPREP version 20.1.3 (Esteban et al., 2019), a Nipype (Gorgolewski et al., 2011) based tool. Preprocessing included the following steps: bias field correction, skull stripping, slice time correction, correction for head motion parameters, co-registration to corresponding structural image, and spatial normalization to MNI space. Each T1w (T1-weighted) volume was corrected for INU (intensity non-uniformity) using *N4BiasFieldCorrection* v2.1.0 (Tustison et al., 2010) and skull-stripped using *antsBrainExtraction.sh* v2.1.0 (using the OASIS template). Brain surfaces were reconstructed using *recon-all* from FreeSurfer v6.0.1 (Dale et al., 1999), and the brain mask estimated previously was refined with a custom variation of the method to

reconcile ANTs-derived and FreeSurfer-derived segmentations of the cortical gray-matter of Mindboggle (Klein et al., 2017). Spatial normalization to the ICBM 152 Nonlinear Asymmetrical template version 2009c (Fonov et al., 2009) was performed through nonlinear registration with the *antsRegistration* tool of ANTs v2.1.0 (Avants et al., 2008), using brain-extracted versions of both T1w volume and template. Brain tissue segmentation of cerebrospinal fluid (CSF), white-matter (WM) and gray-matter (GM) was performed on the brain-extracted T1w using *fast* (Zhang et al., 2001) (FSL v5.0.9). Functional data was slice time corrected using *3dTshift* from AFNI v16.2.07 (Cox, 1996) and motion corrected using *mcflirt* (FSL v5.0.9, Jenkinson et al., 2002). This was followed by co-registration to the corresponding T1w using boundary-based registration (Greve & Fischl, 2009) with nine degrees of freedom, using *bbregister* (FreeSurfer v6.0.1). Motion correcting transformations, BOLD-to-T1w transformation and T1w-to-template (MNI) warp were concatenated and applied in a single step using *antsApplyTransforms* (ANTs v2.1.0) using Lanczos interpolation. Frame-wise displacement (Power et al., 2012) was calculated for each functional run using the implementation of Nipype. Many internal operations of FMRIPREP use *nilearn* (Abraham et al., 2014), principally within the BOLD-processing workflow. For more details of the pipeline see https://fmriprep.readthedocs.io/en/stable/workflows.html.

Correlation matrices were estimated with the *nilearn* Python package (v. 0.7.0; Abraham et al., 2014). To remove physiological and other sources of noise from the fMRI time series, nuisance covariates we regressed out according to the 36-parameter model (Ciric et al., 2017). The fMRI confounds generated with fMRIprep were loaded using the *load_confound* (v. 0.6.4.) Python package. Six motion parameters, signals estimated from cerebrospinal fluid (CSF) and white matter (WM), the whole-brain global signal, their derivatives, quadratic terms, and squares of derivatives were regressed out from functional data separately for each run. The rs-fMRI data was temporally bandpass filtered in the 0.01 – 0.1 Hz frequency range. Global signal regression

(GSR) was performed in line with previous studies on healthy aging (Chan et al., 2014; Malagurski et al., 2020; Ng et al., 2018), as this has been shown to be effective in minimizing the effects of physiological noise and head motion. Further, we used mean framewise-displacement (FD) (Power et al., 2012) as a quality assurance parameter. More specifically, fMRI data were identified as being of low quality if mean FD values exceeded three median absolute deviations (MADs) above the median of the sample distribution across measurement occasions. In total, n = 18 observations were excluded, all of which pertained to individuals with trauma exposure.

Region and Network Definition and Extraction of Connectivity Metrics

The DMN and SN were defined using the Schaefer et al. (2018) parcellation, in which 100 parcels are assigned to 7 well-known resting state networks according to the Yeo-Krienen atlas (Yeo et al., 2011).

Connectivity matrices for each participant and measurement occasion were computed with pairwise correlation between average time series extracted from selected regions. These correlation coefficients were then transformed to z-values using the Fisher's r-to-z transformation.

The DMN comprised the following regions in both hemispheres: parietal cortex, temporal cortex, prefrontal cortex (ventral, dorsal, medial) and precuneus-posterior cingulate cortex. The SN included the right tempro-occipital-parietal region, right frontal-operculum-insula and right medial nodes and left frontal-operculum-insula, left parietal operculum, left prefrontal cortex (lateral) and left medial nodes.

Within-network connectivity was calculated by averaging all ROI-to-ROI connections of a given network. This was done in a stepwise manner. First, pairwise correlations between time series of regions within the two hemispheres and between hemispheres were averaged. In a

second step an average was calculated using these previously computed average connectivity values (average right, average left, average between-hemisphere values). For the between-network connectivity, time series of DMN regions were correlated with time series of SN-regions of the SN; followed by averaging of these pairwise correlations using the same stepwise approach as for the within-network connectivity (i.e. hemisphere-specific averages).

Statistical Analysis

Linear mixed effects (LME) analysis (lme4 package (v. 1.1-18-1) in R (v. 3.5.2); Bates et al., 2014) was performed to assess level and longitudinal change of the within-DMN, within-SN and between-DMN-SN connectivity. As fixed effects we included *time* (baseline, 1-y follow-up, 2-y follow-up, 4-y follow-up, 7-y follow-up), *predtrauma* (individuals with trauma exposure = 1, indivdiuals without trauma exposure = 0) and *predPTSD* (individuals with PTSD symptoms = 1, indivdiuals without PTSD symptoms = 0), as well as their interaction term, in our models. Random effects were subject-specific intercepts and slopes. Additionally, *age at baseline*, *gender* (female = 0, male = 1) and *education* were included as covariates since previous research has shown that age (Malagurski et al., 2020), gender (Tomasi & Volkow, 2011), and education (Chan et al., 2018) are related to the topological organization and functional connectivity of the brain. The dependent variables were within-DMN connectivity, within-SN connectivity, and between-DMN-SN connectivity.

The best-fitting LME was determined via a manual stepwise forward selection procedure. First the random effects structure was determined for which a base model (including only the covariates and a random intercept by subject) was compared to a more complex model including the effect of time, and subsequently to a model including random slopes for participants. Improvements of model fit were assessed using likelihood ratio tests, performed on models fit using maximum likelihood estimation and restricted maximum likelihood

estimation. More specifically, models were compared using the difference $\chi 2$ test, the Bayesian Information (BIS) and the Akaike Information Criterion (AIC). In model comparison, smaller values of BIC ad AIC indicated a better model fit. The significance threshold for the $\chi 2$ test was set to $p < 0.05$.

A similar model fitting procedure (i.e. model comparison) was used to determine if the two predictors – predtrauma and predPTSD – contributed to an improved model fit.

Separate models were fitted for each type of network connectivity (within-DMN, within-SN and between-DMN-SN). In the first step, to describe the connectivity metrics and their trajectories and assess the influence of trauma experience, we ran models that included the full sample. In the second step, to determine if the presence of PTSD symptoms affects resting-state connectivity, we ran additional models that were limited to individuals with trauma exposure. An adjustment for multiple comparisons using the Bonferroni correction was performed. Effect sizes were calculated using the R package *effectsize* by converting F statistics to Eta squared (η^2) (Friedman, 1982).

As the trauma inventory specifically assessed the PTSD symptom expression within the last months and was administered at the 4-year follow-up, an additional multivariate analysis of variance (MANOVA) only using the rs-FC data of the 4-year follow-up (e.g., within-DMN, within-SN and between DMN-SN) as dependent variables, was run for individuals who reported trauma exposure as to examine differences in rs-FC at the 4-year follow-up between individuals who reported PTSD symptoms and individuals without symptoms.

Results

Within-DMN Connectivity

For within-DMN connectivity, the LME model that assumes no change across measurement occasions had the best fit (Supplementary Table 15/16). The baseline model showed a significant effect of gender, qualified by lower within-DMN connectivity in male as compared

to female participants (b = -0.0170, SE = 0.0062, 95% CI [-0.0290, -0.0052], p = 0.0062). There was no evidence for effects of age or education on within-DMN connectivity. In the next modeling step, where trauma exposure was added as a predictor to the model, we found no differences between individuals with and individuals without trauma exposure (p = 0.6384). The effect of gender on within-DMN connectivity, survived the Bonferroni correction (alpha = 0.05/3).

Lastly, the LME model restricted to those individuals who had trauma exposure and including PTSD symptoms as additional predictor showed that within-DMN connectivity was lower for individuals with PTSD symptoms as compared to those not reporting symptoms (b = -0.0215, SE = 0.0091, 95% CI [-0.0387, -0.0043], p = 0.0222) with an effect size of η^2= 0.11, as displayed in Figure 4. The effect of individuals with PTSD symptoms on within-DMN connectivity did not survive the Bonferroni correction (alpha = 0.05/3). There was no evidence for effects of age, gender, or education on within-DMN connectivity. Model estimates are listed in Table 12 and 13.

Within-SN Connectivity

For within-SN connectivity, the LME model that assumes no change across measurement occasions yet again had the best fit (Supplementary Table 17/18). There was no evidence for effects of age, gender, or education on within-SN connectivity. In the next modeling step, individuals with trauma exposure showed a trend for greater within-SN connectivity (b = 0.0175, SE = 0.0103, 95% CI [-0.0173, 0.0229], p = 0.0909) with an effect size of η^2= 0.03.

Lastly, when running an LME model restricted to those individuals who had trauma exposure and including PTSD symptoms as additional predictor, we found no evidence for effects of age, gender or education on within-SN connectivity. Also, the within-SN connectivity was not

lower for individuals with PTSD symptoms (p = 0.5548). Model estimates are listed in Table 12 and 13.

Table 12

Linear Mixed Effect Models of the Within- and Between-Network Connectivity for the Entire Sample N = 110

Network	Predictors	Estimates	SE	Eta squared	CI	*p*
DMN	Age	-0.0009	0.0006	0.02	[-0.0022, 0.0003]	0.1486
	Education	0.0013	0.0035	0.0001	[-0.0055, 0.0081]	0.7144
	Gender	-0.0170	0.0062	0.07	[-0.0290, -0.0052]	0. 0062*
SN	Age	-0.0019	0.0011	0.03	[-0.0039, 0.0002]	0.0885
	Education	-0.0026	0.0060	0.0002	[-0.0141, 0.0089]	0.6621
	Gender	0.0030	0.0104	0.0001	[-0.0170, 0.0230]	0.7849
	predtrauma	0.0175	0.0103	.03	[-0.0173, 0.0229]	0.0909
BN	Age	0.0025	0.0010	0.06	[0.0006, 0.0043]	0.0107*
	Education	0.0002	0.0053	0.0000	[-0.0103, 0.0103]	0.9971
	Gender	0.0436	0.0093	0.18	[0.0256, 0.0612]	< 0.001**
	Time	0.0043	0.0011	0.14	[0.0049, 0.0082]	< 0.001**

Note. Only models with the best model fit indices are shown; *p < .05; **p < .001.

DMN = Default Mode Network, SN = Salience Network, BN = between-network connectivity DMN-SN, predtrauma = individuals with trauma exposure.

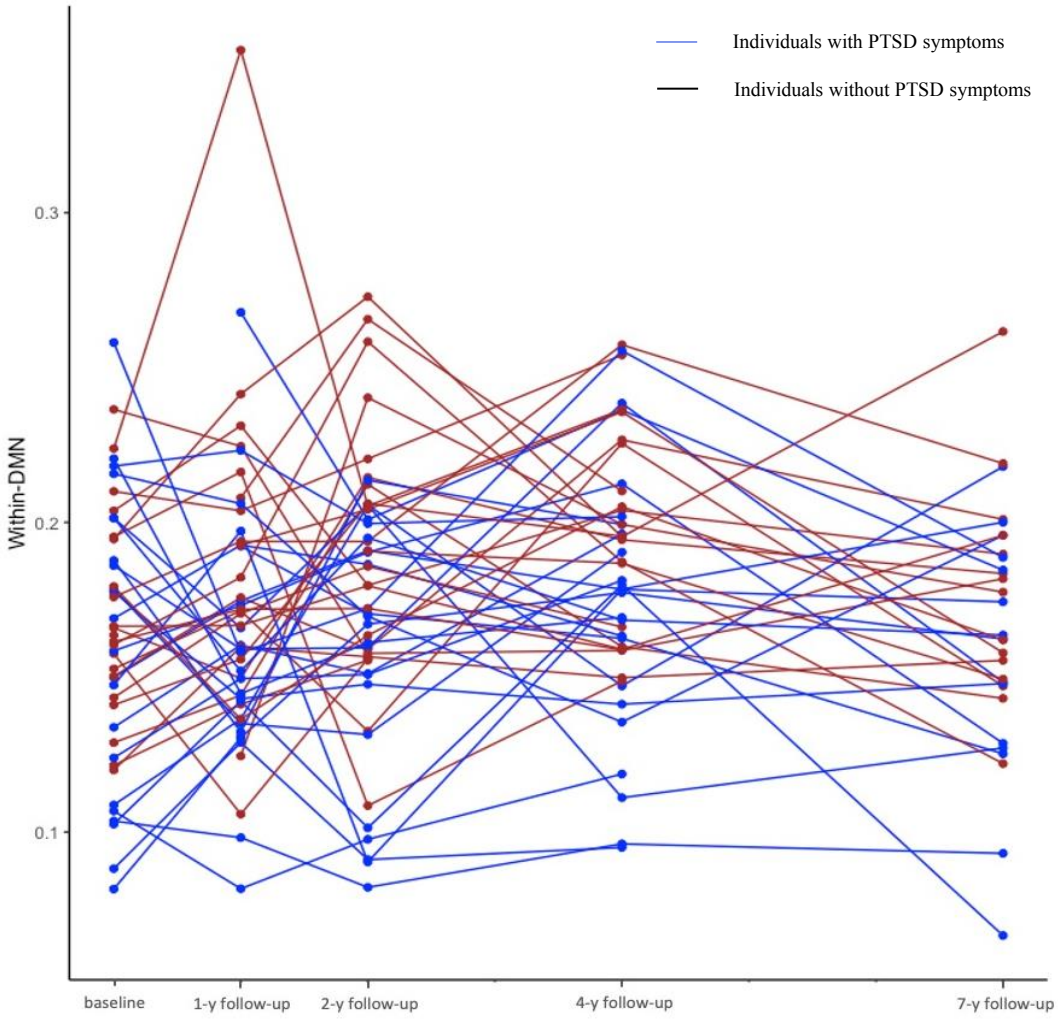

Figure 4. Spaghetti plot of the raw data of the within-DMN connectivity across the five time points. Within-DMN = average connectivity within the Default Mode Network.

Table 13

Linear Mixed Effect Models of the Within- and Between-Network Connectivity for Individuals With Trauma Exposure n = 50

Network	Predictors	Estimates	SE	Eta2	CI	*p*
DMN	Age	-0.0008	0.0009	0.0002	[-0.0026, 0.0010]	0.3914
	Education	0.0031	0.0055	0.0007	[-0.0074, 0.0135]	0.5774
	Gender	-0.0074	0.0094	0.01	[-0.0254, 0.0104]	0.4356
	predPTSD	-0.0215	0.0091	0.11	[-0.0387, -0.0043]	0.0222*
SN	Age	-0.0023	0.0017	0.04	[-0.0056, 0.0010]	0.1914
	Education	0.0013	0.0106	0.0001	[-0.0174, 0.021]	0.8942
	Gender	0.0178	0.0170	0.02	[-0.0153, 0.0497]	0.3004
BN	Age	0.0012	0.0015	0.01	[-0.0018, 0.0041]	0.4175
	Education	-0.0094	0.0089	0.02	[-0.0264, 0.0078]	0.2976
	Gender	0.0491	0.0152	0.19	[0.0201, 0.0787]	0.0023*
	Time	0.0059	0.0014	0.10	[0.0043, 0.0119]	< 0.001**

Note. Only the models with the best fit are shown; *$p < .05$; **$p < .001$.

DMN = Default Mode Network, SN = Salience Network, BN = between-network connectivity DMN-SN, predPTDS = individuals with post-traumatic stress disorder symptoms.

Between-Network Connectivity

For between-network connectivity, the LME model with time as a fixed effect (assuming similar change for all subjects across measurement occasions) had the best fit ($b = 0.0043$, $SE = 0.0011$, 95% CI [0.0049, 0.0082], $p < 0.001$), with an effect size of $\eta^2 = 0.14$ (Supplementary Table 19/20). Furthermore, age ($b = 0.0025$, $SE = 0.0010$, 95% CI [0.0006, 0.0043], $p =$

0.0107) and gender (b = 0.0436, SE = 0.0093, 95% CI [0.0256, 0.0612], $p < 0.001$) had a significant impact on between-DMN-SN connectivity. In the next modeling step, there were no significant differences in the between-DMN-SN connectivity between individuals with or without trauma exposure (p = 0.9844). The effect of age and gender on between-network connectivity survived the Bonferroni correction (alpha = 0.05/3).

Lastly, in the LME model restricted to those individuals who had trauma exposure and including PTSD symptoms as additional predictor, male participants had a higher between-DMN-SN connectivity (b = 0.0491, SE = 0.0152, 95% CI [0.0201, 0.0787], p = 0.0023), whereas age and gender had no effect on between-DMN-SN connectivity. The between-DMN-SN connectivity was not greater for individuals with PTSD symptoms (p = 0.5548) or individuals with trauma exposure (p = 0.9844). The effect of gender on between-network connectivity survived the Bonferroni correction (alpha = 0.05/3). Model estimates are listed in Table 12 and 13.

Post-Traumatic Stress Symptoms and Functional Conncectivity at 4-Year Follow-Up

Comparing individuals with trauma exposure and no PTSD symptoms with individuals with PTSD symptoms on the three functional connectivity metrics at 4-year follow-up narrowly missed significance (F (1, 3) = 4.458, p = .058; Wilk's Λ = .838, partial η^2 = .092). In line with the predictions of the LME models reported above, post-hoc tests reveal the following picture: In comparison to the individuals without PTSD symptoms, individuals with PTSD symptoms showed significantly lower within-DMN connectivity at 4-y follow-up (PTSD symptoms: M = .1723, SD = .0424; no PTSD symptoms: M = .1961 SD = .0334; p = .041), but no differences with regard to within-SN connectivity (PTSD symptoms: M = .2191, SD = .0722; no PTSD symptoms: M = .2124 SD = .0607, p = .550) and between-network connectivity (PTSD

symptoms: *M* = .0398, *SD* = .0725; no PTSD symptoms: *M* = .0217 *SD* = .0758, *p* = .412). See Table 14 for the MANOVA results.

Table 14

Results of a One-Way MANOVA at 4-year Follow Up for Individuals With Trauma Exposure

Network	predPTSD *n* = 24		No predPTSD *n* = 22				
	M	SD	M	SD	F	*p*	Eta^2
DMN	.1723	.0424	.1961	.0334	4.458	.041*	.092
SN	.2191	.0722	.2124	.0607	.363	.550	.008
BN	.0398	.0725	.0217	.0758	.687	.412	.015

Note. *$p < .05$; **$p < .001$; DMN = default mode network, SN = salience network, BN = between-network connectivity DMN-SN, predPTSD = individuals with post-traumatic stress disorder symptoms.

Discussion

Using a non-clinical older adult sample (aged > 65 years) the present study examined differences in within-DMN, within-SN and between-DMN-SN rs-FC in trauma-exposed individuals with and without PTSD symptoms as well as non-trauma exposed individuals. We found that within-DMN connectivity was insensitive to trauma exposure, but lower in individuals who reported PTSD symptoms compared to individuals without symtoms. Within-SN connectivity, on the other hand, was higher in trauma-exposed individuals – independent of whether they reported PTSD symptoms or not – compared to non-trauma exposed individuals.

Although previous studies have reported lower within-DMN connectivity in trauma-exposed individuals, from those studies we cannot conclude whether this stems from the mere exposure to traumatic events or is related to PTSD symptom manifestation (Bluhm et al., 2009; DiGangi

et al., 2016; Sheynin et al., 2020). Our data suggest that lower within-DMN rs-FC is associated with PTSD symptoms manifestation and not with trauma exposure per se (Kunimatsu et al., 2020; Sheynin et al., 2020). Assuming that, in previous studies, the trauma exposure groups had a higher symptom load (e.g., combat-exposed veterans), one could hypothesize that this causes the observed difference between the trauma exposure and non-trauma exposed groups (DiGangi et al., 2016). When symptom load is low, as in our dataset comprising healthy older adults, the symptom-related effect may be masked when only looking at the trauma exposure group as a whole. Our result is also well in line with the fact that DMN activity has been linked to self-referential and other introspective processing (Buckner et al., 2019) possibly pointing towards an abbarent coping mechanism in individuals with PTSD symptoms. Whether the manifestation of PTSD symptoms potentiates the aging effect within individuals over time (causing steeper within-subject slopes) can, however, not be verified in the present study, since our within-DMN models favored stability of rs-FC over change. This stability of rs-FC fits well with the conclusions of a recent review article, in which Jockwitz and collegues conclude that age and aging effects in within-network rs-FC are mostly evident when comparing different age-cohorts while the findings are much less clear in age homogeneous samples of older adults, particularly for within-DMN connectivity (Jockwitz & Caspers, 2021).

With respect to the salience network, we observed greater within-SN connectivity in trauma-exposed compared to non-trauma exposed individuals (trend level) while there was no difference between individuals with and without PTSD symptoms. This may suggest that trauma exposure itself can be associated with functional connectivity changes also in non-clinical older adult poulations. Greater within-SN connectivity in trauma exposued individuals is thought to represent a hyperactivation in response to relevant stimuli but also in a more general way – as an unbalanced attention capturing resulting from an distorted detecting and filtering mechanism of incoming information (Menon, 2011). Several authors even propose

that tackeling within-SN rs-FC may be the working mechanism of action for evidence-based trauma therapy. In more detail, a recent review using MRI to predict cognitive-behavioral therapy outcome and prolonged exposure (guided repeated imaginal and in vivo exposure exercises) (Peterson et al., 2019) showed that a positive treatment response was associated with an improvement in regulating the amygdala by means of the SN (Szeszko & Yehuda, 2019). So far, however, previous research has reported greater within-SN merely in young to middle-aged clinical samples (Sheynin et al., 2020; Stark et al., 2015). Considering the observed trend of increased within-SN rs-FC in trauma-exposed individuals in our non-clinical sample together with the fact that symptoms are often on a subthreshold level in older adults (Pietrzak et al., 2012), future studies should aim to examine bigger non-clinical cohorts as to merit further definite conclusions if within-SN rs-FC is affected by trauma exposure and, thus, deserves further attention in subclinical treatment. As for the within-DMN connectivity, our data do not support significant change of within-SN rs-FC over time. However, the effect of age on within-SN connectivity (i.e., lower connectivity in higher age), although not significant, is consistent with previous work and our hypotheses. Hence, in contrast to the DMN, we see opposing effects of age and trauma exposure. In order to answer the question of how the observed within-SN hyperconnectivity in individuals with a trauma history and the previously reported age-related decline in within-SN rs-FC might co-exist or interact needs further research for clarification.

With respect to between-network connectivity, the present findings do not support an effect of trauma exposure or PTSD symptom manifestation on rs-FC in our subclinical sample of older adults. Our models solely supported a gradual increase of between-DMN-SN connectivity across time in the full sample, which is consistent with previous rs-FC findings in health aging (Chan et al., 2014; Geerligs et al., 2015; Malagurski et al., 2020; Song et al, 2014; Zonneveld et al., 2019). However, trauma exposure or symptom manifestation were not

associated with between-network connectivity changes across time. As suggested in a recent review on MRI findings in PTSD, between-network connectivity may change as a function of the time period during which the trauma exposure occurred (Kunimatsu et al., 2020). More precisely, it has been shown that lower between-network connectivity is associated with early-life trauma (Bluhm et al., 2009), whereas greater between-network connectivity is observed in veterans with trauma exposure in later life (Sripada et al., 2012). Unfortunately, the design and sample size of the present study does not allow to investigate if the time period of trauma exposure may be a moderator. Hence, it is possible that in our study opposing effects diminished a potential influence of trauma exposure or PTSD symptoms on between-DMN-SN rs-FC. Future investigations are encouraged to improve our knowledge of how the communication between networks is affected by trauma exposure and PTSD symptom manifestation as to better understand the role of the time period during which trauma exposure occurred.

Fail to the grasp of complexity, in the present study some limitations need to be considered when interpreting our findings. First, the sample size was relatively small. Future studies collecting and retaining larger cohorts with and without PTSD symptoms following trauma-exposure, should be considered. Despite the comparably small sample size, 45.5% of the individuals in our sample reported to having been exposed to at least one potentially traumatic event. This is slightly lower than in a previous population based study (Glaesmer et al., 2010) who reported rates of 59.7% - 64.3% of exposure to potentially traumatic events in their older adult sample (aged > 60 years). However, given the fact that, historically, the Swiss population was less affected by World War II related trauma exposure as compared to the German older adult sample, the lower exposure rates in the present sample seems reasonable (Glaesmer et al., 2010). Second, the present sample was composed of non-clinical older adults, hence no definite conclusions can be drawn with regard to rs-FC and clinical diagnostic status.

It should be considered that frequency and intensity of reported symptoms was low in the present sample. Although 50% of the trauma-exposed individuals reported at least one symptom that is linked to PTSD, only two participants would meet common diagnostic criteria for PTSD (Siegrist & Maercker, 2010). Previous studies have observed prevalence rates of 0.7% for PTSD and 4.2% of subsyndromal PTSD in older age (65 to 96 years old) (Maercker et al., 2008), which is in line with our data. Third, the trauma exposure and post-traumatic stress measures were only assessed at the 4-year follow-up and participants were asked to indicate symptom manifestation within the last 4 weeks. One might argue, that this does not permit to use PTSD symptoms in our longitudinal dataframe. However, since the three most prominent forms of PTSD in older age are 1) exposure to a traumatic event within the last two years, 2) chronic PTSD following early life adversity and 3) delayed onset PTSD (Maercker, 2021), which are most probable associated with symptom manifestation over a longer time period, we are confident that this does not significantly affect our analyses. Furthermore, we performed an additional analysis specific for the 4-year follow-up measurement occasion, which gave comparable results and, thus, supports the above given interpretation.

To summarize, in this study we, for the first time, investigated the differential effects of trauma exposure and PTSD symptom manifestation on rs-FC and its change within individuals in a non-clinical sample of older adults. Observed trends fit well with the previous observations in clinical samples of individuals with PTSD showing disturbances of self-perception and consciousness associates with altered within-DMN rs-FC and hence help to further our understanding regarding the neural basis of PTSD. Moreover, present findings may help to underscore the importance of studying the magnitude of a traumatic event in non-clinical populations given the observed trend for altered within-SN connectivity in the present sample as to understand potential implication of trauma exposure without significant symptom manifestation over the life span. Altogether, present results suggest that alterations in within-

DMN and within-SN rs-FC can also be observed in non-treatment seeking older adult populations following trauma exposure and in association with PTSD symptoms.

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7 APPENDIX

7.1 **Appendix A:** Supplementary Material to Manuscript 3.

Table 15

Default Mode Network Model Comparison and the Trauma Predictor

Model	Description	-2LL	df	AIC	BIC	Pr(>Chisq)
Random Part						
M1	Random intercept	903.05		-1794.1	-1769.1	
M2	Time	903.08	1	-1792.2	-1762.9	.8236
M3	Random slope	903.15	2	-1788.3	-1750.7	.9307
Fixed Part						
M3a	Predtrauma	903.16	1	-1792.3	-1763.1	.6384

Note. -2LL = log likelihood regression, df = degrees of freedom, AIC = Akaike-Information-Criterion, BIC = Bayesian-Information-Criterion, Pr(>Chisq) = Chi-squared test, predtrauma = individuals with trauma exposure.

Table 16

Default Mode Network Model Comparison and the Post-Traumatic Stress Predictor

Model	Description	-2LL	df	AIC	BIC	Pr(>Chisq)
Random Part						
M1	Random intercept	400.14		-788.27	-768.05	
M2	Time	400.18	1	-786.36	-762.77	.8236
M3	Random slope	400.39	2	-782.78	-752.44	.9307
Fixed Part						
M3b	PredPTSD	403.08	1	-792.16	-768.57	0.01523 *

Note. -2LL = log likelihood regression, df = degrees of freedom, AIC = Akaike-Information-Criterion, BIC = Bayesian-Information-Criterion, Pr(>Chisq) = Chi-squared test, predPTDS = individuals with post-traumatic stress disorder symptoms.

Table 17

Salience Network Model Comparison and the Trauma Predictor

Model	Description	-2LL	df	AIC	BIC	Pr(>Chisq)
Random Part						
M4	Random intercept	693.79		-1375.6	-1350.5	
M5	Time	694.33	1	-1374.7	-1345.4	.300
M6	Random slope	695.04	2	-1372.1	-1334.5	.493
Fixed Part						
M6a	Predtrauma	695.30	1	-1376.6	-1347.4	0.08254

Note. -2LL = log likelihood regression, df = degrees of freedom, AIC = Akaike-Information-Criterion, BIC = Bayesian-Information-Criterion, Pr(>Chisq) = Chi-squared test, predtrauma = individuals with trauma exposure.

Table 18

Salience Network Model Comparison and the Post-Traumatic Stress Predictor

Model	Description	-2LL	df	AIC	BIC	Pr(>Chisq)
Random Part						
M4	Random intercept	304.70		-597.41	-577.19	
M5	Time	304.76	1	-595.53	-571.93	.7332
M6	Random slope	305.01	2	-592.02	-561.69	.7800
Fixed Part						
M6b	PredPTSD	304.88	1	-595.76	-572.16	.5548

Note. -2LL = log likelihood regression, df = degrees of freedom, AIC = Akaike-Information-Criterion, BIC = Bayesian-Information-Criterion, Pr(>Chisq) = Chi-squared test, predPTDS = individuals with post-traumatic stress disorder symptoms.

Table 19

Between Network Model Comparison and the Trauma Predictor

Model	Description	-2LL	df	AIC	BIC	Pr(>Chisq)
Random Part						
M7	Random intercept	738.72		-1465.4	-1440.4	
M8	Time	767.81	1	-1521.6	-1492.4	< .001
M9	Random slope	769.35	2	-1520.7	-1483.1	.2149
Fixed Part						
M9a	Predtrauma	767.82	1	-1517.7	-1480.1	.9844

Note. -2LL = log likelihood regression, df = degrees of freedom, AIC = Akaike-Information-Criterion, BIC = Bayesian-Information-Criterion, Pr(>Chisq) = Chi-squared test, predtrauma = individuals with trauma exposure.

Table 20

Between Network Model Comparison and the Post-Traumatic Stress Predictor

Model	Description	-2LL	df	AIC	BIC	Pr(>Chisq)
Random Part						
M7	Random intercept	318.00		-624.00	-603.77	
M8	Time	326.77	1	-639.53	-615.94	< .001
M9	Random slope	329.16	2	-640.31	-609.98	.09159
Fixed Part						
M9b	PredPTSD	328.16	1	-638.31	-607.98	.249

Note. -2LL = log likelihood regression, df = degrees of freedom, AIC = Akaike-Information-Criterion, BIC = Bayesian-Information-Criterion, Pr(>Chisq) = Chi-squared test, predPTDS = individuals with post-traumatic stress disorder symptoms.

8 CURRICULUM VITAE & PUBLICATION LIST

8.1 Curriculum Vitae

1. PERSONAL INFORMATION, INCLUDING THE RESEARCHER ID

CARLA MAREN EISING, M.Sc.
Phone: +41 77 929 50 26; Email: c.eising@psychologie.uzh.ch

Date of birth: 18.12.1992; Civil / family status: Single; Nationality: German

ORCiD: https://orcid.org/0000-0003-1895-7751

ResearchGate Profile: https://www.researchgate.net/profile/Carla_Eising

UzH Profile: https://www.psychologie.uzh.ch/de/bereiche/hea/psypath/Team/Eising-Carla.html

2. EDUCATION

09/2018- today	***Ph.D. in Psychology***: in progress. Title: "Mental, cognitive, physical, and neurobiological health in aged individuals following the exposure to potentially traumatic events". Department of Psychology, Psychopathology and Clinical Intervention, University of Zürich (UZH), CH (Advisor: Prof. A. Maercker, Ph.D. and M.D.).
	Ph.D. Program in Psychology, in progress. Department of Psychology, UZH, CH.
03/2020- 08/2020	***Research internship,*** Freie Universität zu Berlin (FU), DE, (Advisor: Prof. M. Voelkle, Ph.D.).
09/2016- 08/2018	***Master of Science*** (MSc), in Cognitive and Clinical Neuroscience with the specialization Psychopathology, Maastricht University, NL, (cum laude).
03/2018- 08/2018	***Research internship,*** Stanford University, Stanford Psychiatry Department in collaboration with the VA Palo Alto, US, (Advisor: Prof. D. Spiegel, Ph.D. and M.D., Dr. P. Bayley, PhD.).
	Master Thesis, Title: "Yoga therapy for chronic pain in Gulf War Illness using structural and functional imaging" (Grade: 9). (Advisor: Prof. D. Spiegel, Ph.D. and M.D.).
11/2017- 02/2018	***Clinical internship,*** Personality Disorders and PTSD, Charité Berlin, Campus Benjamin Franklin, DE, (Advisor: Prof. S. Röpke, Ph.D and M.D.).
	Minor Thesis , Title: "Verbal fluency and motor deficits in autism spectrum disorder" (Grade: 9) (Advisor: Dr. F. Ehlen, Dr. B. Behnia).
08/2017	***Summer research internship,*** Mindfulness-based cancer recovery (MBCR), University of Calgary, CA, (Advisor: Prof. L. Carlson, Ph.D.).
09/2013 - 08/2016	***Bachelor of Science*** (BSc), Faculty of Psychology and Neuroscience (FPN), with MaRBLe Honors Research Program (= Minor I), taught in Dutch, Maastricht University, NL.
09/2015 - 12/2015	***Research internship,*** Positive Psychology, Université du Québec à Montreal (UQUAM), CA, (Advisor: Dr. J. Belanger, PhD.).
09/2015 - 12/2015	***Exchange Semester,*** at Departement de Psychologie, taught in French, Université de Montreal (UdeM), CA.

3. EMPLOYMENT HISTORY INCLUDING CURRENT POSITION(S)

11/2020 – today	***Psychotherapist,*** Psychotherapeutic Outpatient Center, Zürich, CH.
09/2018 – today	***Ph.D. student and assistant***, Department of Psychology, Clinical Psychology and Psychotherapy, UZH (Prof. A. Maercker, Ph.D. and M.D), SNSF funded by NRP 76 project "Differential aging trajectories in high-risk individuals with past experiences of early adversity", Prof. A. Maercker, Ph.D. and M.D., Dr. Myriam Thoma.
10/2018- to date	***Climbing instructor,*** Kletterzentrum Gaswerk Zürich, CH.
03/2015- 11/2017	***Climbing instructor.*** UM Sports Maastricht University, NL.

4. INSTITUTIONAL RESPONSIBILITIES	
02/2019- 06/2019	***Organization social events,*** academic mid-level faculty (UZH).
06/2020- 06/2021	***LIFE Fellow Speaker Zürich*** (International Max Planck Research School on the Life Course; participating institutions MPI for Human Development, Humboldt-Universität zu Berlin, Freie Universität Berlin, University of Michigan, University of Virginia, University of Zurich).

5. CO-SUPERVISION OF JUNIOR RESEARCHERS AT GRADUATE AND POSTGRADUATE LEVEL	
12/2020- to date	***Master thesis,*** Nora Brenneisen.
10/2020- to date	***Master thesis,*** Vera Tommer.
05/2019- 12/2020	***Master thesis,*** Carmen Frey.
01/2019- 01/2020	***Master thesis,*** Julienne Buess.
02/2021- 06/2021	***Bachelor thesis,*** Fabienne Joos.
02/2020- 06/2020	***Bachelor thesis,*** Renja Annen.
09/2019- 01/2020	***Bachelor thesis,*** Nico Florineth.
09/2019- 01/2020	***Bachelor thesis,*** Yanick Tobler.
12/2020- 06/2021	***Research intern,*** Ronja Schmid.
09/2019- 02/2020	***Research intern,*** Selma Bruggisser.
09/2019- 02/2020	***Research intern,*** Sandro Stutz.

6. TEACHING ACTIVITIES	
02/2019 – 06/2019	***Experimental-psychological internship (ExPra) (Bachelor level seminar)*****,** Department of Psychology, UZH, CH.
09/2018- to date	***Research Colloquium Master level,*** Department of Psychology, UZH, CH.

7. MEMBERSHIPS IN PANELS, BOARDS, ETC., AND INDIVIDUAL SCIENTIFIC REVIEWING ACTIVITIES	
2020	***Global Advances in Health and Medicine***

8. ACTIVE MEMBERSHIPS IN SCIENTIFIC SOCIETIES, FELLOWHSHIPS IN RENOWNED ACADEMIES	
Since 01/2019	***Cognitive Behavior Therapy Training*** at Akademie für Verhaltenstherapie und Methodenintegration (AIM), Zürich and Wil, CH.
Since 11/2018	***Pre-Doctoral Fellow of LIFE*** (International Max Planck Research School on the Life Course; participating institutions MPI for Human Development, Humboldt-Universität zu Berlin, Freie Universität Berlin, University of Michigan, University of Virginia, University of Zurich).
Since 09/2018	***Doctoral member***, in the University Research Priority Program (URPP) "Dynamics of Healthy Aging", UZH, CH.

9. PRICES, AWARDS, FELLOWSHIPS	
02/2021	**Conference grant,** by German Society of Traumatic Stress Studies (*Deutschsprachige Gesellschaft für Psychotraumatologie,* DeGPT), (€ 120).
01/2020	***Mobility Grant,*** by Swiss National Science Foundation, (CHF 4'818.-).
08/2019	***Travel Grant for the European Congress on Clinical Psychology and Psychological Treatment of EACLIPT,*** by Dresden University of Technology, (€ 600.-).
05/2019	***Graduate Campus Travel Grant (GRC),*** by University Zurich, UZH, (CHF 1'400.-).
05/2019	***Gender Equality Grant,*** by Swiss National Science Foundation, (CHF 1'000.-).

01/2019 ***Travel Expenses Contributions,*** by Schweizerische Akademie der Geistes- und Sozialwissenschaften, SAGW, (CHF 1'000.-).

Since 2015 ***Three travel grants***, by Maastricht University (€1'500.-).

8.2 Research Output List

1. PEER-REVIEWED PUBLICATIONS IN INTERNATIONAL SCIENTIFIC JOURNALS

2021

Eising, C. M., Voelkle, M. C., Rohner, S. L., Maercker, A., & Thoma, M. V. (2021). Lifetime post-traumatic stress disorder in older individuals with a history of institutional upbringing in childhood: the role of social acknowledgement and stressful life events. *European Journal of Psychotraumatology*, *12*(1), 1915578. doi:10.1080/20008198.2021.1915578

Thoma, M. V., Bernays, F., **Eising, C. M**., Maercker, A., & Rohner, S. L. (2021) Child maltreatment, lifetime trauma, and mental health in Swiss older survivors of enforced child welfare practices: Investigating the mediating role of self-esteem and self-compassion. *Child Abuse & Neglect*, *113*, 1-15. doi:10.1016/j.chiabu.2020.104925

Thoma, M. V., Bernays, F., **Eising, C. M.,** Pfluger, V., & Rohner, S. L. (2021). Health, stress, and well-being in Swiss adult survivors of child welfare practices and child labor: Investigating the mediating role of socio-economic factors. *Child abuse & neglect*, 104769. doi:10.1016/j.chiabu.2020.104769

2020

Thoma, M. V., Höltge, J., **Eising, C. M.,** Pfluger, V., & Mc Gee, S. L. (2020). Resilience and stress in later life: A network analysis approach depicting complex interactions of resilience resources and stress-related risk factors in older adults. *Frontiers in Behavioral Neuroscience*, *14*, 216. doi:10.3389/fnbeh.2020.580969

Mathersul, D. C., **Eising, C. M.,** DeSouza, D. D., Spiegel, D., & Bayley, P. J. (2020). Brain and physiological markers of autonomic function are associated with treatment-related improvements in Self-Reported Autonomic Dysfunction in Veterans with Gulf War illness: An exploratory pilot study. *Global Advances in Health and Medicine*, *9*, doi:10.1177/2164956120922812

2018

Falkenberg, R. I., **Eising, C.,** & Peters, M. L. (2018). Yoga and immune system functioning: a systematic review of randomized controlled trials. *Journal of behavioral medicine*, *41*(4), 467-482. doi.org/10.1007/s10865-018-9914-y

2. PEER-REVIEWED BOOKS/MONOGRAPHS

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3. PEER-REVIEWED CONFERENCE PROCEEDINGS

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4. CONTRIBUTIONS TO BOOKS

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5. PATENT AND LICENSE

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6. ORAL CONTRIBUTION TO INTERNATIONAL CONFERENCES

2021

Eising, C. M., Voelkle, M. C., Rohner, S. L., Maercker, A., & Thoma, M. V. (2021). Long-term Associates of Child Maltreatment: Lifetime Post-traumatic Stress Disorder, Social Acknowledgement and Stressful Life Events, Academy Max Planck International Research School on Life Course, Michigan, US.

Thoma, M. V., Bernays, F., **Eising, C. M**., Maercker, A., & Rohner, S. L. (2021). *Mental And Physical Health In Swiss Older Survivors Of Enforced Child Welfare Practices,* GSA 2021 Annual Scientific Meeting, US.

Eising, C. M., Voelkle, M. C., Rohner, S. L., Maercker, A., Thoma, M. V. (2021). Long-term associates of childhood maltreatment and social setting for post-traumatic stress disorder in older age, Symposium of clinical psychology and psychotherapy of the DGP's, Mannheim, DE.

Eising, C. M., Voelkle, M. C., Rohner, S. L., Pfluger, V., Maercker, A., Thoma, M. V. (2021). Der Einfluss von kontextuellen Faktoren während und nach fürsorgerischen Zwangsmaßnahmen in Kindheit und Jugend auf die Posttraumatische Belastungsstörung, Jahrestagung DeGPT, Würzburg, DE.

2020

Eising, C. M., Thoma, M. V., Voelkle, M.C., Maercker, A., Pfluger, V., Rohner, S. L. (2020). Investigating the mediating role of stress and resilience following early abuse and neglect on cognitive and physical functioning in older age, Academy Max Planck International Research School on Life Course, Berlin,DE.

Eising, C. M., Voelkle, M.C., Rohner, S. L., Maercker, A., Pfluger, V., Thoma, M. V. (2020). The impact of childhood abuse and neglect on post-traumatic stress disorder over the life course depends on the social setting, Symposium of clinical psychology and psychotherapy of the DGP's, Mannheim, DE.

2019

Eising, C. M., Hoeltge, J., Maercker, A., Thoma, M. V. (2019). Stress exposure, stress vulnerability, and resilience in older adults with a history of childhood trauma**,** EACLIPT, Dresden, DE.

Eising, C. M., Maercker, A., Thoma, M. V. (2019). Stress sensitivity in aged individuals following childhood trauma, Academy Max Planck International Research School on Life Course, Zürich, CH.

Eising, C. M., Hoeltge, J., Mc Gee, S. L., Thoma, M. V. (2019). Resilience and stress sensitivity following childhood trauma in aged individuals, SGP, Bern, CH.

Eising, C. M., Hoeltge, J., Maercker, A., Thoma, M. V. (2019). Resilience and stress sensitivity following childhood trauma in aged individuals, ESTSS, Rotterdam, NL.

Eising, C. M., Hoeltge, J., Maercker, A., Thoma, M. V. (2019). Differential aging trajectories in high-risk individuals with past experiences of early adversity, Academy Max Planck International Research School on Life Course, Michigan, US.

Eising, C. M., Thoma, M. V., Maercker, A., Martin, M., Jäncke, L., Mérillat, S. (2019). The Impact of Traumatic Experiences on the Normative Aging Process: A Neuroimgaing Investigation, Aging and Cognition, Zürich, CH.

Mathersul, D. C., **Eising, C. M.,** DeSouza, D., Spiegel, D., Bayley, P. (2019). Brain structure and skin conductance predicts treatment-related improvements in autonomic dysfunction in veterans with Gulf War Illness, SANS 2019, Miami, US.

7. OUTREACH ACTIVITIES

2021

Introduction evening on mental disorders for actors – students from the Zurich University of Arts

8. GENERAL CONTRIBUTIONS TO SCIENCE

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9. OTHER ARTEFACTS WITH DOCUMENTED USE

2015

Bélanger, J. J., Nociti, N., Chamberland, P. E., Paquette, V., Gagnon, D., Mahmoud, A., **Eising, C.,** & Kruglanski, A. W. (2015). Building a Resilient Community within a Multicultural Canada: Information Toolkit on Violent Extremism.